

Rapid Review of the literature: Assessing the infection prevention and control measures for the prevention and management of COVID-19 in health and care settings

Publication date: 23 July 2020

Version history

Version	Date	Summary of changes
1.0	19/3/2020	Assessment of the emerging COVID-19 evidence base, includes literature identified up to 16 March 2020.
1.1	3/4/2020	Assessment of the emerging COVID-19 evidence base, includes literature identified up to 30 March 2020.
1.2	20/4/2020	Assessment of the emerging COVID-19 evidence base, includes literature identified up to 13 April 2020.
3.0	15/5/2020	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 11 May 2020.
4.0	24/6/2020	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 15 June 2020.
5.0	23/7/2020	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 20 July 2020

Contents

Abbreviations.....	4
1. Aim	5
2. Objectives.....	5
3. Search Strategy.....	5
Evidence updates.....	6
Results	6
4. Epidemiology.....	7
Transmission routes	7
Clinical presentation	9
Atypical presentations	12
Asymptomatic transmission.....	12
Pre-symptomatic transmission.....	13
Nosocomial transmission.....	13
Incubation period.....	16
Infectious period	16
5. Personal protective equipment	19
Surgical face masks	19
Respiratory protective equipment (RPE)	21
UK PPE guidance.....	21
6. Hand hygiene	24
7. Survival in the environment.....	25
8. Environmental decontamination.....	26
9. Areas for further research	29
References.....	30

Abbreviations

ABHR	Alcohol based hand rub
AGP	Aerosol-generating procedure
FFP2	Filtering face piece respirator (class 2)
FFP3	Filtering face piece respirator (class 3)
FRSM	Fluid-resistant surgical face mask
HDU	High dependency unit
HPS	Health Protection Scotland
ICU	Intensive care unit
ITU	Intensive therapy unit
MERS-CoV	Middle East respiratory syndrome coronavirus
NIPCM	National Infection Prevention and Control Manual
NERVTAG	New and Emerging Respiratory Virus Threat Assessment Group
PPE	Personal protective equipment
RPE	Respiratory protective equipment
SARS-CoV	Severe acute respiratory syndrome coronavirus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

1. Aim

To provide a rapid review of the scientific evidence base to inform the infection prevention and control measures required for the prevention and management of COVID-19 in health and care settings.

2. Objectives

Objectives for the rapid review were to establish the following:

- The epidemiology of COVID-19;
- The personal protective equipment (PPE) requirements;
- The requirements for hand hygiene;
- The environmental survivability of COVID-19;
- The requirements for cleaning/decontamination of the care environment;

3. Search Strategy

Academic databases were searched on 5th March 2020 to identify relevant literature and additional hand searching was conducted. As this was a rapid review, evidence was critiqued but not formally graded with the use of an appraisal tool.

The search terms were as follows:

1. COVID-19.mp.
2. SARS-CoV-2.mp.
3. 2019-nCoV.mp.
4. novel coronavirus.mp.
5. exp coronavirus/
6. 1 or 2 or 3 or 4 or 5
7. exp infection control/
8. exp disinfection/
9. exp decontamination/
10. exp personal protective equipment/
11. surgical mask?.mp.
12. surgical mask?.mp.
13. hand hygiene.mp.
14. clean*.mp.

15.transmission.mp.

16.7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15

17.6 and 16

18.limit 17 to English language

19.limit 18 to yr="2020 -Current"

Evidence updates

The emerging evidence base on COVID-19 is rapidly changing. To account for this, published literature will be screened on a weekly basis and monthly evidence updates produced. Updates to the rapid review will be made as emerging evidence arises and if the evidence base indicates that a change to recommendations is required.

Results

An overarching limitation of all identified evidence is the novel nature of SARS-CoV-2 and the limited ability for robust research at the early stages of an outbreak. Most papers highlight the need for further research.

4. Epidemiology

Transmission routes

The transmission of COVID-19 is thought to occur mainly through respiratory droplets generated by coughing and sneezing, and through contact with contaminated surfaces. Preliminary evidence indicates the routes of transmission to be droplet¹⁻¹⁰ and contact.^{1, 3, 6-11} Evidence also supports indirect contact.^{1, 6, 7, 9, 10} These transmission routes are supported by National¹²⁻¹⁴ and international guidance.^{15, 16}

Currently there is no clear evidence of airborne transmission of SARS-CoV-2. Air sampling studies conducted in COVID-19 hospital environments have shown mixed results; collection of 10 active air samples from ICUs treating COVID-19 patients returned negative results for the presence of viral RNA by RT-PCR.¹⁷ Samples were collected 2-5 metres from the beds of severe/critical patients; patients were either intubated or wore oxygen masks, rooms were mechanically ventilated and a number of patients coughed during sample collection. Negative results were returned following active air sampling (n=16) performed in single patient rooms housing COVID-19 patients both intubated and non-intubated, in multi-bed bays accommodating COVID-19 patients on respiratory treatments deemed likely to generate aerosols e.g. non-invasive ventilation, and in the general corridor outside the rooms of COVID-19 patients in a Dublin hospital.¹⁸ Air sampling using settle plates in a Wuhan hospital failed to detect any viral RNA in general isolation wards, ICUs, fever clinics, ED, treatment rooms, or throat swab sampling rooms; patient-specific details were not provided in this study.¹⁹ Active air sampling, placed 0.6 m away from each patient and 1 m above the floor in 6 negative pressure isolation rooms in China (12 ACH; 1, 2 and 3 person capacity) occupied by 13 COVID-19 patients returned negative results.²⁰ All 13 patients had mild disease and had varying duration of symptoms. A further study in Singapore that used active air samplers placed at 3 different heights in the airborne isolation rooms of 3 COVID-19 patients on a general ward, detected viral RNA in samples from 2 of the rooms.²¹ All three patients were coughing on the day of sampling however additional patient-related factors, such as clinical procedures performed and patient movement, were not provided. It was not possible to make any conclusions about viral load in relation to course of illness as samples were only collected at one time point. Active air sampling in 2 Wuhan hospitals demonstrated very low/non-detectable concentrations of airborne viral RNA in COVID-19 ICUs.²² Samples tested positive in PPE-removal rooms, which led the author to suggest resuspension of virus-laden aerosols from the surface of contaminated PPE was contributing to air contamination. Active air sampling in an ICU treating 15 patients with severe disease and in a general ward treating 24 patients with mild disease returned positive results in 35% of samples collected from the ICU and 12.5% of samples from the general ward.²³ Samples were collected 1m from the patients bed, however there is no detail provided regarding the clinical procedures performed during sampling (e.g. AGPs) and it is possible that droplet dispersal was responsible for the air sampling contamination. Active air sampling in an Italian hospital returned positive results from the COVID-19 ICU and patient corridor; samples from 'clean' areas i.e. staff dressing room, were negative.²⁴ Again, there is limited detail about the patient's clinical status and procedures performed. Active air sampling in a London hospital detected viral RNA in samples from multiple patient areas however repeat sampling

returned positive results in 3 areas only.²⁵ When testing was carried out in the presence of tracheostomies, only 1 of 8 samples was positive. Tests have not been able to identify viable virus or viral replication in air samples collected from hospital inpatient rooms.^{25, 26} Notably, there is large heterogeneity in the sampling method employed in these studies, and no recognised standard for air sampling, which may impact the observed outcomes. A major limitation in these studies is the lack of detail regarding the types, timing and duration of clinical procedures carried out, therefore limiting a full understanding of their potential impact on the observed sampling results. Positive air samples from ICUs may be a reflection of the higher aerosol risk that is related to aerosol-generating procedures (AGPs) that are conducted in these high risk clinical settings.

Aerosol-generating procedures have been associated with an increased risk of transmission of previous coronaviruses (SARS-CoV and MERS-CoV)^{16, 27} and a number of AGPs (mostly airway management) have been implicated as risk factors for transmission of SARS-CoV-2 to health and care workers (HCWs)^{9, 28} however attributing risk to specific procedures with any level of certainty is challenging. The concept of an 'aerosol generating procedure' arose following the study of SARS-CoV transmission events where it was observed that a pathogen, which was consistently associated with droplet or contact transmission, appeared to have the potential to infect HCWs via the airborne route during specific procedures. This is reflected in the World Health Organisation's (WHO) definition of an AGP which states that they create the potential for airborne transmission of infections that may otherwise only be transmissible by the droplet route.²⁹ It should also be recognised that as well as producing aerosols, these procedures produce larger droplet particles.³⁰⁻³²

The WHO further defines an AGP as those procedures which result in the production of airborne particles (aerosols).²⁹ Particles which they describe as being <5 micrometres (µm) in size and as such can remain suspended in the air, travel over a distance and may cause infection if inhaled.²⁹ These particles are created by air currents moving over the surface of a film of liquid, the faster the air, the smaller the particles produced.²⁹ Using this definition there are potentially many medical or patient care procedures which could be classed as 'aerosol generating' but whether they lead to an increased risk of respiratory infection transmission is a different and important question. The 2014 WHO guidance is specific in its wording, outlining that *'some procedures potentially capable of generating aerosols are associated with increased risk of SARS transmission to health-care workers'* and they outline that, regarding pandemic and epidemic prone acute respiratory infections, it is for these procedures that airborne precautions should be used.²⁹ Medical and patient care procedures should be assessed based not only on their capacity to generate aerosols but also on their ability to generate infectious aerosols and an association with relevant transmission events. Health Protection Scotland conducted a review of the evidence base for a number of clinical procedures for their consideration as AGPs in relation to increased risk of respiratory infection transmission, in collaboration with the Department of Health and Social Care's New and Emerging Respiratory Virus Threat Assessment Group (NERVTAG).³³ Additional clarity was provided regarding dental procedures and surgical/post-mortem procedures; risk during dentistry is related to the use of high speed devices such as ultrasonic scalers and high

speed drills. In surgery/post-mortem, risk is related to the use of high speed cutting if this involves the respiratory tract or paranasal tissues.

Clinical presentation

Whilst it is apparent that there is variation in the severity and range of symptoms experienced, the most frequently reported symptoms from case and cohort studies include fever and cough.³⁴⁻⁴⁶ Initial UK data also reflects this.⁴⁷ In China, data indicates that pneumonia was the most frequently reported symptom.³⁴ Anosmia and ageusia (loss of smell and taste), although more subjective, have also been reported⁴⁸⁻⁵² and these symptoms were added to the UK's official list of symptoms in May. Paediatric cases tend to have less severe disease, are hospitalised less frequently than adult patients and are less likely to be admitted to ICU.⁵³⁻⁵⁸ Analysis of symptoms in 126 residents from 4 care homes in London found that early onset anorexia had the strongest independent association with a positive RT-PCR test; cough or shortness of breath were also significantly and independently associated, fever, altered mental state, and diarrhoea were not.⁵⁹

It is widely recognised that those individuals with underlying comorbidities (diabetes, cardiovascular disease, lung disease, cancer) have an increased risk of infection, ICU admission and mortality.⁶⁰⁻⁶⁴ Analysis of 36,398 COVID-19 patients demonstrated that 42.5% had one or more pre-existing morbidity; the most common was hypertension (36.4%), cardiovascular disease (11.9%), and diabetes (22.0%) – mortality rate in the cohort was 14.5% (5,310/36,398).⁶³ Higher risk of death was associated with cardiovascular system diseases, immune and metabolic disorders, respiratory diseases, cerebrovascular system diseases, any types of cancer, renal and liver system diseases. Data from a UK cohort has shown that cardiovascular and cerebrovascular disease was significantly more common in patients that had died by 14 days (90% vs 48% in those still alive) and of these congestive cardiac failure was the most notably associated with non-survival (35% vs 11%).⁴⁷ Median age in this study was 75 years. Case fatality was 21%; the authors state this was much higher than that reported by other studies of all hospitalised patients; the age of the cohort was also higher. This was also the case at a South West London hospital in which case fatality was 32.6% in a 500 patient cohort; average age was 69 years (SD 19.23, range 1 week to 88 years).⁶⁵ It is widely recognised that older age groups have higher rates of underlying comorbidities and both have a correlation with a higher risk of COVID-19 mortality. Among paediatric cases, those requiring hospitalisation are significantly more likely to have underlying comorbidities.⁶⁶

Analysis of 53,000 confirmed cases found that 7.7% experienced gastrointestinal symptoms, with approximately 5.7% experiencing diarrhoea.⁶⁷ The incidence of diarrhoea is more variable in smaller cohort studies (2-50%).^{36, 38, 41, 47, 56, 62, 68-75} Nausea and vomiting are also infrequently reported (5.0% of 1099 confirmed cases from Mainland China).^{75, 76} A number of early papers cited the need for more research into the possibility of faecal-oral transmission^{2, 6, 7, 9-11, 77, 78} following the discovery of viral RNA in the stool samples of COVID-19 patients.^{57, 79-84} Early studies reported on single patient cases^{79, 80, 82, 85} and/or lacked robust clinical data^{79, 81, 86} (i.e. time course of illness, incubation period) which limited interpretation of the epidemiological significance of clinical samples. A pooled detection rate of viral RNA

in stool samples from 436 cases was 43.7%.⁸⁷ Evidence has shown that viral RNA can be detected in stool in both children and adults after clearance in respiratory samples,^{71, 75, 88} in the absence of positive respiratory samples,⁸⁹ and following resolution of symptoms.^{83, 84, 90, 91} It is possible that the presence of viral RNA in stool is due to clearance from the mouth/throat into the gastrointestinal tract from swallowing. The transmission risk from non-respiratory samples is still being investigated. Initial attempts at live virus isolation from stool were unsuccessful,⁹² however live virus has since been isolated from a stool sample taken approximately 19 days after symptom onset from a severe COVID-19 patient (who subsequently died) in China.⁹³ Following inoculation of Vero E6 cells, a cytopathic effect was observed after two days, and viral particles with the typical morphology of the SARS-CoV-2 virus was observed. Live virus has also been isolated from 62 samples collected from 23 patients using Vero cells; median duration of shedding was 8 days post symptom onset and the probability of detecting isolated virus dropped below 5% after 15.2 days post symptom onset (95% confidence interval (CI) 13.4 – 17.2).⁹⁴ The sample size in this preprint study was very small and further prospective studies that assess time course of viral shedding in relation to illness progression in individual cases is required. Wolfel et al, in the absence of histopathology, analysed the presence of viral sgRNA in clinical samples, which is only transcribed in infected cells and therefore can indicate the presence of actively-infected cells.⁹² They reported 'no or only minimal' indication of replication in stool by this method however this was a small study (n=9) and an area of research that requires further work. Limited data from endoscopic examination of infected patients has revealed positive staining of viral host receptor ACE2 in gastrointestinal epithelial cells, leading to the suggestion that gastrointestinal cells are actively infected⁸⁴ however this is a single study and an area of research that requires further investigation. To date there is no evidence of direct human-to-human transmission from faecal material.

It is worth noting that the application of standard infection control precautions (SICPs) would prevent ongoing transmission via the faecal-oral route.

Viral RNA has also been detected in blood samples from infected patients.^{81, 95-99} However transmission risk via the blood would be expected to be very low and transmission via this route has not been previously reported for respiratory viruses.

Viral RNA has not been detected in vaginal fluid,¹⁰⁰ testicular biopsy samples¹⁰¹ or expressed prostatic secretion¹⁰² in the small number of those tested although has been detected in semen both during infection and after symptom resolution.¹⁰³ Semen samples from 34 Chinese males taken 1 month after COVID-19 diagnosis were all negative,¹⁰⁴ as was a sample taken 8 days post symptom onset from a single case with mild infection.⁵⁰ Semen samples from a cohort of 20 German males including 2 with active infection and 18 in the convalescent phase (8-54 days after absence of symptoms) all tested negative.¹⁰⁵ Urine samples have tested positive in a small number of cases.^{97-99, 106} Viral load in urine was low but detectable and cytopathic effects were observed 3 days after inoculation onto Vero E6 cells¹⁰⁶ but in a separate study, inoculation onto CaCo-2 cells did not yield results.⁹⁹ These findings do not indicate infection of the kidneys or bladder however there is a possibility of transmission via the urine.

Peritoneal fluid collected during emergency appendicectomy tested negative for viral RNA.¹⁰⁷

SARS-CoV-2 has been detected in the tears and conjunctival secretions in COVID-19 patients with conjunctivitis^{4, 108-113} and without,¹¹¹⁻¹¹⁵ leading to the suggestion that transmission could be possible via the mucous membranes and secretions of the eyes.^{116, 117} All secretions (except sweat) and excretions from patients with known or suspected COVID-19, should therefore be regarded as potentially infectious.

There is limited evidence regarding mother-to-child transmission. The majority of studies describe development of COVID-19 in the third trimester with subsequent caesarean deliveries and no evidence of vertical transmission.¹¹⁸⁻¹²⁶ There is less evidence for vaginal births but the majority have reported no evidence of vertical transmission.¹²⁶⁻¹³⁴ Seven rapid systematic reviews found no clear evidence of vertical transmission.^{130, 135-140} Two neonates have tested positive by RT-PCT 24 hrs after birth (1 caesarean, 1 vaginal) with additional positive obstetric tissue samples (amniotic fluid, placenta); only one neonate developed fever at birth, the other remained asymptomatic and neither had respiratory symptoms.^{141, 142} Nine reports describe positive neonatal samples in 17 neonates within 36 hrs of birth but obstetric samples were either not collected¹⁴³⁻¹⁴⁷ or tested negative.^{119, 148-150} In these studies, the majority of neonates (14/17) were delivered by caesarean section; the majority of mothers (9/10) had mild infection (1 severe, 7 unreported) and all were in the late 2nd or 3rd trimester. Placental/membrane samples have also tested positive but in the absence of positive neonatal RT-PCR results.¹³² Antibody testing conducted in neonates has demonstrated mixed results; positive IgM and IgG tests in a number of cases,¹⁵¹ however in one neonate born to a mother with severe infection, both neonatal IgM and IgG tests were negative.¹⁴⁴ Amongst a cohort of 11 infants born to mothers with COVID-19, all had detectable IgG (100%) and 5 (45.5%) had detectable IgM at birth; RT-PCR test results were all negative.¹⁵² The majority of studies which have tested obstetric samples have not been able to detect viral RNA in amniotic fluid, cord blood, placenta, or breast milk in those tested.^{128, 129, 135, 136, 138, 153} Three cases of positive breast milk have been reported; RT-PCR testing from a sample taken 1 day after delivery was positive however repeat sampling 2 days later was negative.¹⁵⁴ In a separate case, samples taken 10 days post birth were positive but subsequent tests on days 14-25 were negative.¹⁵⁵ A third case describes positive viral samples from breast milk of an asymptomatic mother, ingested by a neonate became SARS-CoV-2 positive at 9h hrs post-vaginal delivery, however alternative transmission routes could not be ruled out.¹⁵⁶ Transmission events from breast milk have not been reported. The WHO recommend that mothers with suspected or confirmed COVID-19 should be encouraged to initiate or continue to breastfeed.¹⁵⁷ One neonate delivered vaginally in Italy developed symptoms and tested positive 3 days after birth but it is not clear if the baby was isolated from the mother after birth.¹⁵⁸ Whilst many studies describe IPC and isolation measures put in place during and following birth, it is possible that COVID-19 may have been transmitted to neonates from routes other than vertical; immediate testing on delivery may provide more clarity. Overall, evidence suggests very low risk of vertical transmission.

Atypical presentations

Atypical presentations include cases that do not display the typical clinical symptoms (fever, cough) (which constituted the case definition to date) but may test positive or show radiographic abnormalities (i.e. ground-glass opacity). The absence of respiratory symptoms/fever has been reported in children^{44, 53, 58, 95, 159-161} and adults^{37, 72, 162}, with diagnosis often relying on RT-PCR and radiological investigation. Conjunctivitis in the absence of any other symptoms has also been reported.^{110, 163} An atypical presentation occurred in an Italian national evacuated from China and quarantined on arrival with 56 others as a precautionary measure.⁸⁵ This case was a healthy 28 year old male who had no respiratory symptoms but had mild conjunctivitis and slight tonsillar exudate in the presence of positive naso- and oro-pharyngeal samples and stool samples. The risk of transmission from these individuals, and whether it differs from that of individuals with typical presentations, has not been determined.

A rare Kawasaki-like disease has been identified in a small number of children presenting with COVID-19 in multiple countries.^{164, 165} Presence of body and acral rashes with or without additional symptoms has been reported.¹⁶⁶ Hormati et al provide a brief report on the admission of two patients to a gastroenterology clinic in Iran with unusual gastrointestinal symptoms; both tested positive for COVID-19 in the absence of respiratory symptoms or fever.¹⁶⁷ Again, no transmission events were reported from these patients. A case report describes possible transmission from a 94 year old patient with atypical presentation (delirium, abdominal pain).¹⁶⁸ Nine HCWs and another inpatient developed COVID-19 after the patient was treated in three wards over 5 days with no infection control precautions, highlighting that there is risk of transmission from atypical presentations where no precautions are taken. Based on the increasing number of reports of atypical presentation, it may be pragmatic to consider widening the case definition as more evidence arises.

Asymptomatic transmission

A study by Ma et al (*not peer-reviewed*) that assessed clinical symptoms reported by 7 countries, calculated that, among RT-PCR-positive cases with relevant information (n=329), 49 (15%) were asymptomatic however it was not stated if radiographic symptoms were present.³⁵ Smaller studies have also reported positive asymptomatic cases, identified during contact tracing, that remained asymptomatic up until the point of negative RT-PCR conversion.¹⁶⁹⁻¹⁷¹ or for the duration of a specified follow-up period.¹⁷² Universal screening of 52 asymptomatic obstetric patients in Japan identified low prevalence in the cohort (3.8%); all cases remained asymptomatic.¹⁷³ To date, there has been limited evidence of transmission from positive-asymptomatic cases. A number of studies report on identification of viral RNA in clinical samples in asymptomatic patients,^{90, 95, 172, 174-177} and contact tracing has identified possible transmission from a small number of these cases.^{49, 176} Contact tracing identified a possible asymptomatic index case in a family cluster in China¹⁷⁶ and in Vietnam;⁴⁹ both cases had normal CT imaging and no symptoms. It would appear that asymptomatic cases appear to be younger.¹⁷⁸ A growing number of paediatric cases have been reported detailing asymptomatic presentations with positive clinical samples however transmission events from these cases could not be proven.^{44, 54, 58, 90, 95, 170, 174, 179-181} The proportions of asymptomatic-

positive cases are difficult to contextualise due to a lack of point-prevalence-type data from asymptomatic individuals in the wider community.

Pre-symptomatic transmission

Possible transmission in the incubation period has been reported in a number of studies, mainly small cluster case reports.^{175, 182-189} A recent report detailed possible pre-symptomatic transmission in 7 community case clusters in Singapore; date of exposure could be determined in 4 clusters which suggested transmission occurring 1-3 days prior to symptom onset from source patients.¹⁸³

Rothe et al report a single case of a Chinese national that travelled to Germany for business and reported hearing coughing from the rows behind on the airplane but was asymptomatic for the duration of contact with German colleagues.¹⁷⁵ Having developed symptoms on return to China, contact tracing was carried out and two German colleagues were identified as positive with mild symptoms. A cluster of cases in Germany developed from this travel-related cluster and a further pre-symptomatic transmission event was identified between 2 individuals that met in a work canteen; this transmission event was strongly supported by virus sequence analysis.¹⁸⁷

Contact during the incubation period during a conference was identified as a possible mode of transmission from a single person to 2 family clusters in China; symptoms in the index case developed 2 days after the conference.¹⁸⁴ Transmission in a cluster of young people (16-23yr olds) in China was linked to an asymptomatic index case who had contact with all persons in the cluster; all cases including the index case subsequently developed symptoms.¹⁸⁵ The estimated incubation period was notably short (median 2 days) in this study. Two further cases of pre-symptomatic transmission were implicated in familial clusters in China; both cases had contact with a pre-symptomatic individual from Wuhan.¹⁸⁴ Gao et al also describe possible pre-symptomatic transmission in the incubation period in a cluster of community cases.¹⁸⁶ As with the aforementioned studies, there were no severe or critical patients in this cohort.

It is notably that these studies did not have clinical data available in the incubation period and relied on contact tracing analysis. As clinical sampling may not be widely conducted on mild/community-based cases (or asymptomatic individuals), there may continue to be a paucity of data in relation to determination of asymptomatic/pre-symptomatic transmission. The majority of evidence to date continues to point towards transmission occurring predominantly during the symptomatic period.

Nosocomial transmission

Data regarding symptoms in HCWs is limited but suggests a mirroring of symptoms experienced by the community/general population.¹⁹⁰ In a Dutch cohort of 86 COVID-19-positive HCWs, the majority suffered relatively mild disease and 93% met a case definition of fever and/or coughing and/or shortness of breath.¹⁹¹ Other symptoms included headache, runny nose, sore throat, chest pain, and diarrhoea. A large proportion (63%) of those screened worked whilst being symptomatic, therefore the possibility of HCW-HCW and HCW-

patient transmission (or indeed community transmission) cannot be ruled out, especially considering only 3% reported exposure to a positive inpatient.

There are reports of clear nosocomial transmission during the earlier stages of the epidemic.¹⁹² A COVID-19 outbreak on the paediatric dialysis unit of a German hospital involved transmission from an index patient to 7 HCWs and 3 patients.¹⁹³ Transmission from an undiagnosed neurosurgery patient to 12 HCWs occurred at a hospital in Wuhan; appropriate PPE was not worn, with many HCWs not wearing surgical masks.¹⁹⁴ Possible transmission from an undiagnosed patient to 3 HCWs was suspected to have occurred when performing a bronchoscopy ('procedure' masks were worn, not respirators), however genetic sequencing was not carried out and contact tracing is not described in detail.¹⁹⁵ A case report describes possible transmission from a 94 year old patient with atypical presentation (delirium, abdominal pain) to 9 HCWs and another inpatient after the patient was treated in three wards over 5 days with no infection control precautions.¹⁶⁸ Reports from a South West London hospital revealed that 51 of 500 analysed admissions developed COVID-19 nosocomially while inpatients.⁶⁵ A separate inpatient cohort (n=435) from a London teaching hospital reported that 47 cases over a 6 week period met the definition for definite hospital acquisition (symptom onset 14 days or more after admission); many of these cases were identified as having been in the same bay or ward as a patient with PCR-confirmed COVID-19.¹⁹⁶ Nosocomial transmission from an unknown individual to a patient in an ITU, with subsequent transmission to 5 patients and 16 HCWs within the ward, occurred at a tertiary care university hospital in the UK. The infection cluster occurred after hospital visits were stopped and at the same time as lockdown was announced.¹⁹⁷ A lack of social distancing between staff may have contributed to transmission, as the working environment did not allow it; unfortunately WGS was not carried out in this study therefore it was not possible to analyse the transmission events with greater clarity. Research conducted in March/April with NHS England Trusts to inform the Scientific Advisory Group for Emergencies (SAGE) suggests that nosocomial transmission of COVID-19 is occurring, with 8.2% of cases being diagnosed 14 days post-admission (inter-quartile range 3.8% to 12.0%). It was reported that few Trusts are assessing the possible involvement of HCWs in transmissions.

As sustained community transmission has occurred as the pandemic has progressed, it has become more challenging to identify true nosocomial transmission events. Screening of 1654 symptomatic HCWs by an English NHS Trust between March 10-31st identified 240 (14%) positive individuals; comparison of rates between staff in patient-facing and non-patient facing roles found no evidence of a difference, suggesting that data may reflect wider patterns of community transmission rather than nosocomial-only transmission.¹⁹⁸ Mirroring of community transmission was also identified at a large public hospital in Madrid,¹⁹⁹ and at three hospitals in the Netherlands; contacts with COVID-19 individuals was reported from out-with the hospital and from contact with colleagues.²⁰⁰ Complete genome sequencing of 50 HCW and 18 patients suggested that the observed patterns were most consistent with multiple introductions into the hospital.²⁰⁰ Genetic sequencing provided confirmatory evidence for community transmission to a HCW, ruling out suspected transmission from two COVID-19 patients.²⁰¹

Whilst transmission from asymptomatic HCWs has not been documented, a UK study identified a small proportion (0.5% of 1,032) of asymptomatic-positive HCWs during a routine screening study, highlighting the risk of transmission from these individuals.²⁰² HCWs working in 'red' or 'amber' wards were significantly more likely to test positive than those working in 'green' wards ($p=0.0042$) – this was the case for both symptomatic and asymptomatic-positive HCWs. A smaller UK study that routinely tested a cohort of asymptomatic HCWs on a weekly basis identified 44/400 (27%) that tested positive in the absence of symptoms in the week before or after positivity.²⁰³ Results from the study suggest a likely reflection of general community transmission, however it does raise concern about the risk of nosocomial transmission from these individuals. Data from 4 London care homes identified 44 residents that were asymptomatic-positive and remained so when tested a week later; as symptom history was not obtained prior to testing, it is possible that these individuals may have been post-symptomatic at time of first testing with an unusually prolonged viral shedding.⁵⁹ Some SARS-CoV-2 sequence variants were highly similar between residents and/or staff within a single care home; there were also multiple distinct clusters of SARS-CoV-2 sequence types within single nursing homes, suggestive of multiple introductions. At a long term nursing facility in the US, 13 residents were asymptomatic-positive during a point prevalence test and remained so over a 30 day follow up, but again, symptom history pre-testing was not obtained.²⁰⁴

It is notable that not all unprotected exposures to COVID-19-positive individuals result in transmission; none of the 21 HCWs that reported contact with an undiagnosed patient with mild respiratory symptoms at a Swiss hospital tested positive when tested 7 days later.²⁰⁵ The patient underwent routine clinical examinations, blood draws, electrocardiograms, chest X-rays and had nasopharyngeal swabs taken; masks were never worn by HCWs during the patient's care. In Germany, a physician worked over a number of days in a hospital whilst symptomatic (coughing, fever) and with no mask, but did not transmit infection to any of the 254 identified contacts (HCWs and patients).²⁰⁶ In Singapore, 41 HCWs were exposed to multiple AGPs at a distance of less than 2 metres for at least 10 minutes while wearing predominantly surgical masks (only 25% wore N95 respirators) whilst caring for a patient with undiagnosed COVID-19; none of the HCWs developed symptoms or tested positive (with repeat testing) in the 14 days following exposure.²⁰⁷

Conclusion:

- Standard Infection Control Precautions (SICPs) should always be applied in all situations regardless of the infectious nature of the patient.
- Droplet precautions should be implemented when in close contact (within 2 metres), or providing direct patient care to a suspected/confirmed COVID-19 patient.
- Airborne precautions should be implemented when undertaking an AGP on a suspected/confirmed COVID-19 patient.

Incubation period

Many of the studies published to date are limited by small sample sizes and over-representation of severe cases, the incubation period for which may differ from that of mild cases. Evidence suggests an incubation period of 5-6 days^{7, 10, 45, 62, 74, 187, 190, 208-221} with a range of 1-14 days^{7, 8, 11, 38, 41, 62, 76, 190, 211, 212, 214, 215, 222-224} from infection to symptoms surfacing. Further analysis of 2,555 Chinese community cases indicates a longer incubation period of 9 days.²²⁵ Lauer et al estimate that most (97%) of those who develop symptoms do so within 11.5 days of infection (95% CI, 8.2-15.6), consequently only a limited number of cases will potentially develop symptoms out-with the 14 days of self-isolation that is required following contact with a confirmed case.²¹⁰

Conclusion:

- The incubation period for most individuals is reported as 5-6 days (range 1-14 days).
- Self-isolation for 7 days is recommended for individuals with symptoms consistent with COVID-19.
- Self-isolation for 14 days is recommended for contacts of symptomatic cases.

Infectious period

In most cases, individuals are usually considered infectious whilst they have respiratory symptoms; how infectious an individual is likely depends on the severity of their symptoms and stage of their illness. Initial data from Wuhan suggested a median time from symptom onset to clinical recovery for mild cases of approximately 2 weeks, and 3-6 weeks for severe or critical cases however this data is likely biased by the fact that the majority of cases included in the study were hospitalized therefore the proportion of milder community cases may be underestimated.²¹¹

Less is known about the duration of infectivity. From limited international data, the balance of evidence is that, for mild cases of infection, infectivity (as determined by respiratory RT-PCR sampling) peaks at symptom onset and significantly reduces 7 days after the onset of symptoms but appears to take longer for severe cases.^{92, 211, 226-229} Community transmission on the day of symptom onset (when symptoms are mild and non-specific) has been reported but is reliant on retrospective self-reported data.²³⁰ Analysis of 301 hospitalised cases revealed that the positive rate of RT-PCR assay was highest at day 0-7 (97.9 %) after symptom onset then decreased with time; after 4 weeks, 26.3% of samples were still positive.²³¹ It was also observed that patients ≥ 65 years old shed virus for longer (22 days vs 19 days, $p=0.015$). Prolonged detection of viral RNA up to 28 days after symptom onset has also been reported from hospitalised cohorts.^{52, 232, 233} Analysis of a US cohort of 121 patients and HCWs demonstrated an average time of 24 days after symptom onset for transition from RT-PCR positive to negative; 10% remained positive 33 days after symptom onset.²³⁴ Details of symptoms and infection severity were not reported, however there is evidence that patients with severe infection (requiring ICU admission) shed virus (as detected in nasal swabs) for significantly longer than non-ICU patients.¹¹⁵ Cohort studies (limited by their small sample sizes) have shown that patients discharged from hospital can continue to

have viral RNA detected in respiratory and stool samples for more than 14 days.^{235, 236} This prolonged viral shedding may not represent transmissible infectious viral cells; there is limited evidence regarding this. Wolfel et al assessed 9 cases in Munich, Germany and found that live virus could be isolated from respiratory samples taken within the first 7 days of symptoms but not from day 8 onwards, even though viral RNA could still be detected in samples.⁹² Live virus isolation may also be dependent on viral load; samples containing under 10^6 copies/mL (or copies per sample) never yielded an isolate.⁹² In the absence of histopathology, the same study analysed the presence of viral sgRNA which is only transcribed in infected cells and therefore can indicate the presence of actively-infected cells in samples. Throat swabs taken up to day 5 were positive while no sgRNA was detected thereafter. This single study suggests that as viral load reduces in the later stages of infection, so too does transmission risk. Wolfel et al estimate that, for patients beyond day 10 of symptoms and with less than 100,000 viral RNA copies per ml of sputum, early discharge with ensuing home isolation might be appropriate.⁹²

Virus has also been isolated from the nasopharyngeal samples of 12 symptomatic children (age range 7 days-15.9 years), however as consecutive sampling was not carried out (cases were outpatients or isolating at home), it was not possible to assess infectivity over the course of disease.²³⁷ Further research is required in the area of viral isolation to develop a robust evidence base. The infectious dose required for transmission has yet to be determined.

Data from a number of studies has demonstrated a pattern with viral clearance with regards to clinical sample type; viral presence in respiratory samples appears to peak in the earlier stages of infection then decreases with time whilst the opposite has been observed with stool samples.^{83, 84, 90, 98} Analysis of hospitalized cases in China indicated an association between hypertension and delayed viral clearance.^{227, 238} Hypertension is the most frequently reported CV comorbidity associated with COVID-19 infection; hypertensive patients also have a higher mortality rate compared to normotensive patients.⁶⁰ This has led to the suggestion that treatment with ACE2 inhibitors (antihypertensive medication) in patients with hypertension might facilitate SARS-CoV-2 to enter the targeted cells via ACE2 receptors in the respiratory system, and thus prolong the time of viral clearance.²²⁷ Further research is required to detangle the association between severe disease, comorbidities, and delayed viral clearance.

Reports that suggest possible infectivity in the asymptomatic period are based on limited evidence from largely retrospective observations during contact tracing, and identification of viral RNA in clinical samples post symptom resolution.^{10, 83, 95, 174, 175, 222, 239-241} Concerns over risk of transmission in the incubation period have been raised following observations of positive clinical samples prior to symptom onset. Unfortunately, contact tracing studies frequently lack accompanying clinical data i.e. RT-PCR testing from the incubation period, due to their retrospective nature. A report from a long term care facility in which two rounds of 'point prevalence' COVID-19 screening were carried out (1 week apart), found that more than half the residents (27 of 48) who had positive tests were asymptomatic at testing.²⁴² Further, 17 of 24 specimens (71%) from pre-symptomatic persons (those who were asymptomatic at testing but went on to develop disease) had viable virus by culture 1 to 6 days before the development of symptoms. Possible transmission events from these

individuals were not reported. Identification of RT-PCR positivity in the incubation period has also been reported in South Korea; 41 out of 213 tested (19.2%) were asymptomatic at testing.²⁴³ Progression to disease was not reported; all individuals were isolated therefore transmission events in this cohort were not assessed.

Knowledge is also limited regarding the transmission dynamics of asymptomatic-positive cases. Analysis of the initial RNA load and threshold cycle value ('Ct' value, which is inversely proportional to the viral load) from a number of small studies indicates a lower viral load in asymptomatic cases during hospitalisation.^{98, 177, 193} In one study, symptomatic cases had an approximately 200-fold higher viral load.¹⁹³ However, a larger study found that the initial threshold cycle value of nasopharyngeal RNA in asymptomatic carriers was similar to that in pre-symptomatic and symptomatic patients, but that viral clearance was faster, as the RNA negative-conversion occurred earlier for asymptomatic cases.¹⁷⁹ From this, the authors deduced that the communicable period of asymptomatic cases was shorter than pre-symptomatic patients (9.63 days vs. 13.6 days). Significantly faster viral clearance in asymptomatic cases has been demonstrated in a number of small studies.^{49, 177} Analysis of 82 Chinese cases found that those with respiratory symptoms (cough) had a statistically significantly longer duration of positive testing by nasopharyngeal swab compared to patients presenting without respiratory symptoms (17 days vs. 13 days, $p = 0.041$).²⁴⁴

In general, the evidence regarding the transmission dynamics from asymptomatic cases is weak; further research is required.

Guidance from the ECDC recommends that COVID-19 patients may be discharged from hospital based on: a) clinical resolution of symptoms, and b) evidence for viral RNA clearance which would be 2 negative RT-PCR tests from respiratory specimens at 24 hrs interval at least 8 days after onset of symptoms, where testing capacity permits.²⁴⁵ However in light of the widespread community transmission, clinical criteria should gain priority. This is consistent with Scottish and UK guidance which recommends discharge as soon as the patient is clinical well enough (i.e. symptoms may still be present).^{246, 247} Those discharged should self-isolate for 7 days (with absence of fever for 48 hours) and 14 days (with absence of fever for 48 hours) for patients who received critical care and/or are immunocompromised.^{246, 247}

Conclusion:

- Transmission is most likely to occur whilst an individual is symptomatic.
- In mild cases of infection, where hospitalisation is not required, the risk of transmission is thought to significantly reduce after 7 days.
- In severe cases the risk of transmission may extend beyond 7 days therefore Transmission Based Precautions (TBPs) should remain in place for the duration of hospital admission or home isolation until cessation of symptoms.
- In hospital settings clinicians should consider extending isolation for some cases e.g. elderly, immunosuppressed, if they remain symptomatic after 14 days until test results are available.

- Patients discharged from hospital should self-isolate for 7 days (14 days if critical care was received) with absence of fever for 48 hours.

5. Personal protective equipment

There was limited evidence for the assessment of the PPE requirements for the prevention of transmission of SARS-CoV-2. Determination of the PPE requirements for new pathogens is usually based on previous experience with similar pathogens and/or similarly-transmitted pathogens. Determination of the efficacy of PPE recommendations is based on retrospective analyses of possible transmission events to HCWs, where any associations with PPE worn at the time are assessed. Such assessments are considered to be low quality evidence and prone to confounding.

Surgical face masks

It is vital that a distinction is made between the evidence pertaining to fluid-resistant surgical face masks (FRSM) (Type IIR) and standard (non-fluid-resistant) surgical face masks (Types II). Surgical masks are tested against the safety standard BS EN 14683:2019; this series of tests measures the performance of a surgical mask in bacterial filtration efficiency (BFE), breathing resistance and splash resistance. Type II and Type IIR surgical masks are both tested against this standard with them needing to meet a minimum BFE of 98%; however only Type IIR masks must pass the splash resistance test with a resistance of at least 16.0kPa. The terms 'fluid resistant' and 'fluid repellent' are often used interchangeably to denote a Type IIR surgical mask, however, terminology may vary internationally and a 'fluid repellent' mask may occasionally describe a mask that does not meet the BS EN 14683:2019 splash resistance standard and which is not suitable for protection against splash or spray i.e. a Type II surgical mask. In the UK, when recommended for infection prevention and control purposes a 'surgical mask' will be a fluid-resistant (Type IIR) surgical mask.

Standard surgical face masks (i.e. Type II) can be worn by an infectious individual to prevent transmission.²⁴⁸⁻²⁵⁰ To demonstrate this, a study by *Leung et al* tested the efficacy of surgical masks at reducing the detection of seasonal (non-COVID-19) coronavirus in exhaled breath from infected patients.²⁵¹ Coronavirus could be detected in ~40% of samples collected from non-mask wearers (n=10) but was not detected in exhaled air from patients that wore surgical masks (n=11). The masks used were Type II, i.e. they were not fluid-resistant. This study was limited by the small sample size – due in part to the fact that a large proportion of infected participants had undetectable viral shedding in exhaled breath. Studies assessing Type II surgical masks have also reported reduced detection of seasonal influenza in exhaled breath in mask wearers.^{251, 252} An environmental sampling study of multiple sites (prior to environmental cleaning) surrounding 3 hospitalised COVID-19 patients yielded negative results; two of these patients wore surgical masks continually and the critical bed-bound ICU patient had a closed loop circuit ventilator.²⁵³ All patients tested positive by throat swab on the day of sampling and the masks and the closed suction tube tested positive.

Whereas standard surgical face masks can be worn by an infectious individual to prevent transmission, it is the fluid-resistant nature of FRSMs that provides additional protection to the wearer (e.g. HCW) against droplet-transmitted infectious agents. Guidance consistently

recommends that HCWs should wear a Type IIR FRSM as PPE when caring for a patient known, or suspected, to be infected with an infectious agent spread by the droplet route.^{29, 248, 250, 254-258} In UK health and care settings, surgical masks must be fluid-resistant, 'CE' marked and compliant with Medical Device Directive (MDD/93/42/EEC) and the Personal Protective Equipment Regulations 2002.²⁵⁹⁻²⁶⁴

Surgical masks do not provide protection against airborne particles and are not classified as respiratory protective devices.²⁶⁵ Assessment of PPE use against similar coronaviruses i.e. severe acute respiratory virus (SARS), provides weak evidence that droplet precautions (i.e. surgical masks) are adequate. A systematic review and meta-analysis combining 6 case-control and 3 cohort studies, found that use of respirators/masks provided significant protection against SARS-CoV among exposed HCWs (OR=0.22; 95% CI: 0.12-0.40). Wearing surgical masks (OR=0.13; 95% CI: 0.03-0.62) or N95 respirators (OR=0.12; 95% CI: 0.06-0.26) (versus no RPE) both reduced the risk of SARS-CoV by approximately 80%. No protective effect was reported for disposable cotton or paper masks. The existing evidence base in the review was sparse and the indications (and compliance) for mask/respirator use varied between the included studies.²⁶⁶ The type of surgical mask was not reported in all studies. A case control study that compared PPE use in 241 non-infected HCWs and 13 infected HCWs with documented exposure to 11 index patients with SARS-CoV found that none of the infected staff wore surgical masks or respirators (2 wore paper masks).²⁶⁷ However, RT-PCR analysis was not used to confirm infection in this study (confirmation of HCWs relied on serological analysis), and recall bias for PPE use may have affected results. Inadequate reporting of RPE/mask indications and compliance was a major limitation in a recent systematic review and meta-analysis conducted by *Bartoszek et al*, which included 4 RCTs and reported that, compared to N95 respirators, the use of medical masks was not associated with an increase in laboratory-confirmed viral respiratory infection or respiratory illness.²⁶⁸ There was significant variation in surgical mask type between the included studies (Type IIR FRSMs were not used in every study). A rapid review conducted specifically to assess the RPE requirements for COVID-19 in primary care determined that the evidence base was weak as the included studies were focussed on influenza transmission, not COVID-19; these studies provided weak support for the use of standard surgical masks in non-AGP settings.²⁶⁹ A recent update to a Cochrane systematic review that assessed full body PPE for the prevention of exposure to highly infectious diseases (including COVID-19) found that covering more parts of the body leads to better protection but usually comes at the cost of more difficult donning or doffing and less user comfort, and may therefore even lead to more contamination.²⁷⁰ Certainty of the evidence was judged as low due to the fact that almost all findings were based on one or at most two small simulation studies.

For all non-AGP scenarios, there is no clear evidence that respirators offer any additional protection against droplet-spread infectious disease, including coronaviruses.

Guidance issued by the Scottish Government on 23rd June advises that all staff in hospitals and care homes in Scotland who interact with patients or residents are required to wear a 'medical' face mask throughout their shift, from 29th June onwards.²⁷¹ Patients and visitors to hospitals and care homes are advised to wear a face covering. The main purpose of these measures is to prevent transmission of the virus from the person wearing the face mask, in

recognition of the risk of pre-symptomatic and asymptomatic transmission, and the difficulties in maintaining social distancing in the workplace.

Conclusion:

- Health and care workers in hospitals and care homes should wear a type IIR fluid-resistant surgical face mask throughout their shift; a type II surgical face mask may be worn by HCWs that are not involved in direct patient care/not at risk of splashing/spraying.
- Non-medical staff and HCWs off duty/out-with clinical areas in hospitals and care homes should wear a face covering.
- All patients and visitors entering a hospital or care home should wear a face covering.
- In all other health and care settings, HCWs should wear a type IIR fluid-resistant surgical face mask during any activities/procedures where there is a risk of blood, body fluids, secretions or excretions splashing or spraying onto their nose or mouth and when providing non-AGP care to a patient known or suspected to be infected.
- Symptomatic inpatients may wear either a type II or IIR fluid-resistant surgical mask if they can be tolerated.

Respiratory protective equipment (RPE)

The WHO defines an AGP as a medical or care procedure that creates the potential for airborne transmission of infections that may otherwise only be transmissible by the droplet route.²⁹ It should also be recognised that as well as producing aerosols, these procedures produce larger droplet particles.³⁰⁻³² During AGPs there is an increased risk of aerosol spread of infectious agents irrespective of the mode of transmission (contact, droplet, or airborne) and airborne precautions (FFP3 respirator and facial protection) must be implemented.²⁷²

It is important to note that not all FFP3 respirators are fluid-resistant; valved respirators can be shrouded or unshrouded. Respirators with unshrouded valves are not considered to be fluid-resistant and therefore should be worn with a full face shield if blood or body fluid splashing is anticipated. This must be taken into consideration where FFP3 respirators are being used for protection against COVID-19 transmission.

Conclusion:

- Airborne precautions (FFP3 respirators) are required at all times when providing care in high risk units ('AGP hotspots') and when performing AGPs on patients with suspected/confirmed COVID-19.

UK PPE guidance

For general patient care (i.e. non-AGP situations), the first edition of the UK IPC pandemic COVID-19 guidance initially recommended type IIR FRSMs, disposable aprons and disposable gloves.¹⁴ The decision to wear eye protection was based on risk assessment (but considered essential when carrying out AGPs). Fluid-resistant long sleeve gowns were recommended for management of confirmed cases and when carrying out AGPs.¹⁴ FFP3

respirators were recommended when carrying out AGPs and when in high risk areas where AGPs are being conducted. The FFP3 recommendation was based on expert opinion from NERVTAG which recommended that airborne precautions should be implemented at all times in clinical areas considered AGP 'hot spots' e.g. Intensive Care Units (ICU), Intensive Therapy Units (ITU) or High Dependency Units (HDU) that are managing COVID-19 patients (unless patients are isolated in a negative pressure isolation room/or single room, where only staff entering the room need wear a FFP3 respirator).

The UK IPC pandemic COVID-19 guidance was updated on 2nd April 2020 with a move to PPE based on risk of exposure to possible (not suspected/confirmed) cases, with recommended ensembles for specific care areas/clinical situations.²⁷³ The guidance states that *'incidence of COVID-19 varies across the UK and risk is not uniform and so elements of the updated guidance are intended for interpretation and application dependent on local assessment of risk'*. While this is not in line with the evidence base to date for COVID-19 as presented in this rapid review, it is based on the potential challenges in establishing whether patients and individuals meet the case definition for COVID-19 prior to a face-to-face assessment or care episode.

Specifically, FRSMs are recommended for direct patient care (within 2 metres) in inpatient, radiology, maternity and labour wards (2nd/3rd stage labour vaginal delivery – no AGPs), operating theatres (no AGPs), emergency departments/acute assessment areas, and when transferring possible (suspected) or confirmed cases.²⁷³ Either a disposable plastic apron or a fluid-resistant gown can be worn, with the exception being when performing AGPs outside high risk acute care areas, when a gown must be worn. Eye protection (single or reusable full face visor or goggles) is recommended at all times with the exception of inpatient care to any individuals in the extremely vulnerable group undergoing shielding.²⁷³

AGP 'hot-spots', and consequently the locations requiring HCWs to don FFP3 respirators, were expanded to include ED resuscitation areas, wards with non-invasive ventilation, operating theatres, endoscopy units for upper respiratory/ENT or upper GI endoscopy, and any other clinical areas where AGPs are regularly performed.²⁷³

There was also a move towards sessional use of PPE considering the recognised global shortage of PPE stockpiles and perhaps in recognition of the fact that the change in UK PPE recommendations are likely to result in greater use of PPE by a wider staff group which will deplete existing UK stocks.

On April 17th 2020, an additional section was added to the UK IPC pandemic COVID-19 guidance, *'Considerations for acute personal protective equipment (PPE) shortages'* which recommends (in addition to sessional use) reuse of FFP3/FF2/N95 respirators, fluid-resistant gowns or coveralls, goggles and face visors. PPE items which are to remain single-use (and non-sessional) are disposable gloves and aprons.

The safety and efficacy of extended use or re-use of PPE has not been extensively studied. An evidence summary by ECRI (Emergency Care Research Institute), a US company that evaluates medical devices, evaluated 21 laboratory studies and concluded that extended use (i.e. sessional use) of N95 respirators was preferable to reuse.²⁷⁴ Mechanical failure (e.g. broken straps and poor sealing between the mask and the user's face) following only a few

reuses was common across a number of FDA-cleared N95 respirators. The reported pathogen transfer risk from contact during donning and doffing during reuse was considered to be higher than the risk from sessional wear. Use of surgical masks or similar disposable covers over N95s during sessional wear were unlikely to result in significant adverse effects. Reuse would require disinfection however loss of filter performance was reported with some common disinfection methods. The methods for disinfection included humid heat, chemical disinfection, and ultraviolet germicidal irradiation (UVGI). The ECRI report summarises the findings from a number of decontamination studies conducted; steam sterilisation required 10 minutes at a minimum of 121°C to be effective however it may damage polymer fibres in the filter and compromise performance; chemical disinfection was limited by the risk of toxicity and chemical incompatibility with filter materials; UVGI penetration may be incomplete in multi-layered N95 filters. UVGI is capable of inactivating coronaviruses including MERS-CoV and SARS-CoV however these tests were not conducted on any type of PPE.²⁷⁵ UV radiation degrades polymers which presents the possibility that UVGI exposure may reduce the efficacy of respirators.²⁷⁶ A previous study demonstrated degradation of 4 different types of N95 respirators at doses of 120-950 J/cm².²⁷⁷ Attempts at using steam sterilisation of FFP respirators has shown promise however rigorous testing in line with EN standards for respirator efficacy is required.²⁷⁸ None of the eight different decontamination methods tested on different N95 respirator models were suitable, failing in terms of ability to penetrate the filters and/or as a result of damage to the respirators.²⁷⁹ The methods included UVGI, ethylene oxide, hydrogen peroxide gas plasma, hydrogen peroxide vapour, microwave-oven-generated steam, bleach, liquid hydrogen peroxide, and moist heat incubation (pasteurization). Disinfection using aerosolised peracetic acid and hydrogen peroxide vapour was found to be effective at reducing contamination of a surrogate coronavirus bacteriophage on N95 respirators.²⁸⁰ Use of vaporised hydrogen peroxide was also found to be suitable for N95 respirator decontamination using an experimental inoculum of SARS-CoV-2 with a cycle threshold value of 20–22.²⁸¹ Notably, the safety of these chemicals for this purpose has not been tested and decontamination should be tested on naturally contaminated PPE, as experimental contamination may not be representative of the levels of contamination experienced in real-life clinical scenarios.

The extant UK IPC pandemic COVID-19 guidance does not recommend decontamination of respirators.²⁷³ Respirators should be discarded if they become moist, visibly soiled, damaged, or become hard to breathe through. The ECDC recommends that, where reuse of respirators is considered as a last resort option to economise on use of PPE, the risk of the surface of the respirator becoming contaminated by respiratory droplets is considered to be lower when it is covered with a visor.²⁸² However this ensemble is dependent on a plentiful supply of visors.

As highlighted in the ECRI report, the reported pathogen transfer risk from contact during donning and doffing during reuse was considered to be higher than the risk from sessional wear.²⁷⁴ Unfortunately there is no evidence available to assess the impact on filtration efficacy or the risk of transmission associated with reuse of RPE in clinical settings. A study that assessed efficacy of type IIR FRSMs and N95 respirators that were worn sessionally and reused did not include a reliable control group for comparison which prevented assessment

of the efficacy of continuous wear/reuse.²⁸³ RPE was reported to be stored between shifts in a paper bag in lockers; the extent of reuse was not reported. Compared with continuous use of FRSMs, respirators were associated with more problems for the wearer including significantly greater discomfort, trouble communicating with the patient, headaches, difficulty breathing, and pressure on the nose.²⁸³ The WHO '*Rational use of PPE for COVID-19*' mentions that respirators can and have previously been used for extended periods of time to treat multiple patients with the same diagnosis.²⁸⁴ Whilst WHO state that there is evidence to support respirators maintaining their protection over longer periods of time, it may not be comfortable to use one respirator for longer than 4 hours and this should be avoided²⁸⁴ as reuse may increase the potential for contamination and contact transmission of infectious agents (not just SARS-CoV-2). This risk must be balanced against the need to provide respiratory protection for HCWs providing care and to those performing AGPs. To reduce the risk of transmission associated with PPE reuse it is essential that HCWs demonstrate stringent compliance with all other infection control precautions, hand hygiene, and environmental decontamination. Irrespective of the measure implemented, HCWs must have IPC education and training on the correct use of PPE and other IPC precautions, including demonstration of competency in appropriate procedures for donning and doffing PPE and hand hygiene. These issues are for consideration by the Health and Safety Executive (HSE). The HSE approved the sessional use and reuse of PPE in the UK for COVID-19 and expects NHS Boards to have an agreed action plan that includes consideration of all measures to manage usage effectively.

Conclusion:

- Single use eye protection and single use RPE should be worn when performing AGPs.
- Sessional use of respirators is preferred over reuse.
- The decision to reuse PPE (respirators, fluid-resistant gowns or coveralls, goggles and face visors) should be based on a risk assessment considering the care activities, patient population, and the state of the PPE in question.

6. Hand hygiene

Most articles identified recommend that hand hygiene should be performed, however many do not specify the product(s) to be used in preventing the transmission of SARS-CoV-2. A number of guidance documents provide specific recommendations which differ only slightly.^{8, 12, 16} WHO and Public Health England support the use of soap and water, and alcohol-based hand rub (ABHR) when soap and water is not available and when hands are not visibly soiled.^{12, 16} Experimental evidence has shown that commercially-available ABHRs and WHO ABHR formulations are effective at inactivating SARS-CoV-2 within a contact time of 30 seconds.²⁸⁵ Commercially-available ABHRs have also shown efficacy against other coronaviruses included SARS-CoV and MERS-CoV.^{285, 286}

Conclusion:

- Hand hygiene should be performed with soap and water or, when hands are not visibly soiled, with ABHR.

7. Survival in the environment

A number of environmental sampling studies of isolation rooms occupied by COVID-19 patients and surrounding areas sampled various locations prior to environmental cleaning; viral RNA was found on multiple room surfaces including the bed rail, locker, chair, light switches, sink, taps, floor, window ledge, PPE storage area, hand sanitiser dispensers, air outlet fan, elevator buttons, as well as the toilet bowl surface and door handle, and medical equipment (ventilators, monitors, blood pressure cuffs).^{18-21, 23, 24, 26, 287-289} Personal items such as mobile phones and TV remotes were also contaminated.^{26, 288} Positive rates were significantly higher in medical areas compared to office areas and buffer rooms for donning PPE; contamination in these areas was found on telephones, desktops, keyboards, computer mice and water machine buttons.¹⁹ A study that sampled multiple surfaces within an emergency triage unit and a sub-intensive care ward identified positive samples on 2 CPAP helmets only.²⁹⁰ It is possible that environmental cleaning, carried out 4 hours prior, may have impacted results. Environmental sampling studies are often limited as they omit information regarding frequency of environmental cleaning, or conduct sampling immediately following cleaning.^{291, 292} The potential effect of disease progression and viral shedding on environmental contamination has not been investigated extensively, however one study has demonstrated a significant correlation between viral load ranges in clinical samples and positivity rate of environmental samples ($p < 0.001$).²⁹³ When the viral load of clinical samples was higher than or equal to 3 log copies/ml, environmental contamination with SARS-CoV-2 could be detected. However, the sample size in this study was small and further research is required to confirm these findings. Viral samples from environmental sampling were shown not to be viable, in the two studies that assessed this.^{26, 290} In general, these studies highlight the potential for environmental contamination, particularly of frequently-touched areas. An in-vivo study tested the viability of SARS-CoV-2 under a number of experimental conditions and found that cells remained viable for 3-5 days at room temperature.²⁹⁴ In light of limited data for SARS-CoV-2 regarding survival time in the environment, evidence was assessed from studies conducted with human coronaviruses including MERS-CoV and SARS-CoV, and human coronavirus 229E. From largely experimental studies, human coronaviruses are capable of surviving on inanimate objects and can remain viable for up to 5 days at temperatures of 22-25°C and relative humidity of 40-50% (which is typical of air conditioned indoor environments).^{11, 78, 295-298} Survival is also dependent on the surface type.²⁹⁵ An experimental study using a SARS-CoV-2 strain reported viability on plastic for up to 72 hours, for 48 hours on stainless steel and up to 8 hours on copper.²⁹⁹ Viability was quantified by end-point titration on Vero E6 cells. An experimental study conducted with human coronavirus 229E found that the virus persisted on Teflon, PVC, ceramic tiles, glass, and stainless steel for at least 5 days (and 3 days for silicon rubber) at 21°C and a relative humidity of 30-40%.³⁰⁰ Infectivity of the persistent viral cells was demonstrated experimentally using a plaque assay, however the infectivity of surface-contaminating SARS-CoV-2 in real-life remains unknown.

Survival of human coronaviruses and surrogates in water is influenced by temperature (viral inactivation increases with increasing temperatures) and organic or microbial pollution.³⁰¹ A 99.9% viral titre reduction was observed after 2-3 days in waste water in an experimental

study using human coronavirus 229E, suggesting low survivability in waste water.³⁰² Samples taken from the treated sewage outlet of a COVID-19 Chinese hospital were negative.³⁰³ Samples taken (with varying methodology) from external water treatment plants in the Netherlands, France, and the US tested positive in line with the detection of cases in the population which suggests that RT-PCR analysis of sewage could be a potential surveillance tool.³⁰⁴⁻³⁰⁷ Testing of sewage treatment works is now being carried out by the Scottish Environment Protection Agency (SEPA) to determine if such data exists to generate a surveillance system. There is currently no evidence that COVID-19 is transmitted from sewage or contaminated drinking water.³⁰⁸

Conclusion:

- Due to the uncertainty regarding the environmental survivability of SARS-CoV-2 in real-life conditions, it is essential that the environment is clutter free and frequency of routine cleaning is increased, particularly frequently-touched surfaces.

8. Environmental decontamination

Evidence for cleaning of the care environment for COVID-19 is limited; studies that evaluate the susceptibility of coronaviruses to cleaning/disinfectant products differ by their methodology and often use animal coronaviruses in experimental conditions.^{78, 286, 295} An experimental study using a SARS-CoV isolate, tested three different surface disinfectants but all required over 30 minutes exposure time to inactivate the virus to levels below detection.²⁸⁶ Limited evidence suggests that coronaviruses are susceptible to chlorine-based disinfectants and ethanol-based antiseptics.^{295, 309} Kampf et al summarised the efficacy of various disinfectants against both human and animal coronaviruses and found that a concentration of 0.1% sodium hypochlorite was effective in 1 minute and, for the disinfection of small surfaces, 62-71% ethanol revealed a similar efficacy.²⁹⁵ The WHO recommends that, for coronaviruses, commonly used hospital-level disinfectants such as sodium hypochlorite (at a concentration of 0.5%) are effective for cleaning environmental surfaces, and 70% ethanol is suitable for disinfecting small surfaces.¹⁶ A sampling study found that twice daily cleaning of frequently-touched areas using 5000 ppm of sodium dichloroisocyanurate (a source of free chlorine) resulted in negative swab results for COVID-19 in isolation rooms that had just been cleaned; samples taken from rooms prior to cleaning had multiple positive samples from frequently-touched areas.²⁸⁷ Similar results were reported at a Chinese hospital in which surfaces were routinely wiped with 1000 mg/L chlorine-containing disinfectant every 4 hours in isolation ICUs and every 8 hours in general isolation wards; none of the environmental samples in these areas tested positive for SARS-CoV-2 contamination.³⁰³ Negative results were also found from sampling of 90 surfaces following disinfection in a Wuhan hospital dedicated to COVID-19 patients, in which a comprehensive environmental decontamination protocol was implemented.¹⁹⁰ It consisted of chlorine dioxide air disinfection 4 times a day for 2 hours at a time in COVID-19 wards, irradiation of empty wards with UV light once per day for 1 hour, ultra-low volume spraying of chlorine dioxide (500mg/L) for air disinfection in public areas, and surfaces/objects were 'wrapped' with chlorine-containing disinfection solution (1000mg/L) twice a day.

For situations where health and care settings are at capacity and/or have no breaks in admissions or bed occupancy, the opportunity to conduct a terminal clean or a deep clean may be limited. Solutions to this may include modification to the deep clean regime to allow as high a level of decontamination to be carried out during constant occupancy as possible.

In light of the concern raised regarding aerosol transmission following the identification of positive (but not viable) air samples from hospital rooms,^{21, 22, 26, 287} alternative decontamination techniques that offer air decontamination should be explored. Air disinfection using ultraviolet light, termed ultraviolet germicidal irradiation (UVGI) is accomplished via several methods: irradiating the upper-room air only, irradiating the full room (when the room is not occupied or protective clothing is worn), and irradiating air as it passes through enclosed air-circulation and heating, ventilation, and air-conditioning (HVAC) systems.³¹⁰ UVGI is also used in self-contained room air disinfection units. The room/area must be vacated during UVGI decontamination, which might be a problem in health and care settings experiencing constant occupancy, and/or full capacity and thus might be a barrier to the use of UVGI for routine decontamination. However, UVGI may be suitable for routine decontamination of care homes, where communal areas such as dining rooms/activity areas are vacated daily. A study conducted in an American nursing home found that use of a portable UVGI disinfection device for terminal cleaning of resident rooms, and weekly UVGI disinfection of shared areas (dining rooms and activity areas), was significantly associated with reduced respiratory infection rates ($p=0.017$) and hospitalisation by pneumonia ($p=0.006$).³¹¹ There is the possibility that the manual cleaning (using a combined sodium hypochlorite-detergent cleaning agent) that preceded UVGI disinfection may have also influenced the observed infection rate reductions. Whole-room UVGI is capable of inactivating coronaviruses including MERS-CoV and SARS-CoV.²⁷⁵ A review of UV decontamination technology by HPS recommended that UV light systems can be used as an additional measure when performing terminal room decontamination³¹² and this technology is already used in some health and care settings in the UK. Terminal decontamination is essential for reducing the risk of nosocomial transmission to the next room occupant, and will be particularly important as health and care settings begin to re-open.

Research conducted with NHS England Trusts to inform the Scientific Advisory Group for Emergencies (SAGE) suggests that nosocomial transmission of COVID-19 is occurring, with 8.2% of cases being diagnosed 14 days post-admission (inter-quartile range 3.8% to 12.0%). The survey demonstrated variation between Trusts in implementation of the latest IPC guidelines, and poor IPC practice in a number of areas. Concern was voiced regarding the lack of concise and comprehensive cleaning guidelines for COVID-19. Cleaning will be particularly important as outpatient/elective areas begin to re-open. There is an urgent need to address this in UK IPC pandemic COVID-19 guidance.

Conclusion:

- A combined detergent/disinfectant solution at a dilution of 1,000 parts per million available chlorine (ppm available chlorine (av.cl.)) should be used for transmission-based environmental cleaning.²⁷² Small surfaces, and those which cannot be cleaned by chlorine-based agents, can be disinfected with 70% ethanol.

- Frequency of environmental decontamination in COVID-19 areas in all health and care settings should be increased to at least twice daily, focusing on frequently-touched areas.
- Where terminal cleaning cannot be carried out due to constant occupancy, a modified enhanced clean should be carried out where possible.
- The use of UVGI should be considered where possible as part of both routine and terminal cleaning.
- In health and care settings that are COVID-19-free, frequency of routine environmental cleaning (with detergent) should be increased while community transmission is ongoing.

Archive copy only

9. Areas for further research

An overarching limitation of all identified evidence is the novel nature of SARS-CoV-2 and the limited ability for robust research at the early stages of an outbreak.

More work is needed to improve and develop culture techniques to allow determination of the viability of viral particles detected in clinical and environmental samples. This will assist with determination of the infectious dose and will provide insight into the duration of infectivity, particularly in relation to the prolonged viral shedding that is observed in faecal samples.

Further research is required to determine the extent of atypical presentations, pre-symptomatic, and asymptomatic transmission and the overall impact of these on transmission. A robust epidemiological evidence base will assist with the development of infection control measures that are targeted and evidence-based.

Assessment of the efficacy of UVGI and other novel decontamination technologies for environmental decontamination and for the decontamination of PPE would inform COVID-19 IPC guidance and provide reassurance for health and care workers.

References

1. To KKW, Tsang OTY, Chik-Yan Yip C, et al. Consistent detection of 2019 novel coronavirus in saliva. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2020; 12.
2. Wang FS and Zhang C. What to do next to control the 2019-nCoV epidemic? *The Lancet* 2020; 395: 391-393. Note.
3. Rothan HA and Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *Journal of Autoimmunity* 2020: 102433. Review.
4. Xia J, Tong J, Liu M, et al. Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection. *Journal of Medical Virology* 2020; 26: 26.
5. Peeri NC, Shrestha N, Rahman MS, et al. The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned? *International journal of epidemiology* 2020; 22.
6. Yang Y, Shang W and Rao X. Facing the COVID-19 outbreak: What should we know and what could we do? *Journal of medical virology* 2020; 24.
7. Lai CC, Shih TP, Ko WC, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *International Journal of Antimicrobial Agents* 2020; (no pagination). Review.
8. Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Military Medical Research* 2020; 7 (1) (no pagination). Review.
9. Wax RS and Christian MD. Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patients. *Canadian Journal of Anesthesia* 2020. Review.
10. Wu YC, Chen CS and Chan YJ. Overview of The 2019 Novel Coronavirus (2019-nCoV): The Pathogen of Severe Specific Contagious Pneumonia (SSCP). *Journal of the Chinese Medical Association : JCMA* 2020; 11.
11. Li JY, You Z, Wang Q, et al. The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future. *Microbes and infection* 2020; 19.
12. Public Health England. COVID-19: infection prevention and control guidance. 6 March 2020 2020.
13. Department of Health Ireland. COVID-19 (Coronavirus): Advice. How COVID-19 (Coronavirus) spreads. 10 March 2020 2020.
14. Department of Health and Social Care (DHSC) PHWP, Public Health Agency (PHA) Northern Ireland, Health Protection Scotland (HPS), Public Health England,. COVID-19; Guidance for infection prevention and control in healthcare settings. 2020.
15. Centres for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19) – How COVID-19 Spreads. Centres for Disease Control and Prevention, 2020, p. <https://www.cdc.gov/coronavirus/2019-ncov/about/transmission.html>

16. World Health Organization. Infection prevention and control during health care when coronavirus (nCoV) infection is suspected. Interim guidance. 25 January 2020 2020.
17. Faridi S, Niazi S, Sadeghi K, et al. A field indoor air measurement of SARS-CoV-2 in the patient rooms of the largest hospital in Iran. *Sci Total Environ* 2020; 725: 138401. 2020/04/14. DOI: 10.1016/j.scitotenv.2020.138401.
18. Jerry J, O'Regan E, O'Sullivan L, et al. Do established infection prevention and control measures prevent spread of SARS-CoV-2 to the hospital environment beyond the patient room? *J Hosp Infect* 2020 2020/06/27. DOI: 10.1016/j.jhin.2020.06.026.
19. Wu S, Wang Y, Jin X, et al. Environmental contamination by SARS-CoV-2 in a designated hospital for coronavirus disease 2019. *Am J Infect Control* 2020 2020/05/15. DOI: 10.1016/j.ajic.2020.05.003.
20. Wei L, Lin J, Duan X, et al. Asymptomatic COVID-19 Patients Can Contaminate Their Surroundings: an Environment Sampling Study. *mSphere* 2020; 5 2020/06/26. DOI: 10.1128/mSphere.00442-20.
21. Chia PY, Coleman K, Tan YK, et al. Detection of air and surface contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in hospital rooms of infected patients. *medRxiv* 2020; NOT PEER REVIEWED.
22. Liu Y, Ning Z, Chen Y, et al. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. *Nature* 2020 2020/04/28. DOI: 10.1038/s41586-020-2271-3.
23. Guo ZD, Wang ZY, Zhang SF, et al. Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020. *Emerg Infect Dis* 2020; 26: 1583-1591. 2020/04/11. DOI: 10.3201/eid2607.200885.
24. Razzini K, Castrica M, Menchetti L, et al. SARS-CoV-2 RNA detection in the air and on surfaces in the COVID-19 ward of a hospital in Milan, Italy. *Sci Total Environ* 2020; 742: 140540. 2020/07/04. DOI: 10.1016/j.scitotenv.2020.140540.
25. Zhou J, Otter JA, Price JR, et al. Investigating SARS-CoV-2 surface and air contamination in an acute healthcare setting during the peak of the COVID-19 pandemic in London. *medRxiv* 2020; PREPRINT. DOI: <https://doi.org/10.1101/2020.05.24.20110346>.
26. Santarpia J, Rivera D, Herrera V, et al. Transmission potential of SARS-CoV-2 in viral shedding observed at the University of Nebraska Medical Centre. *medRxiv* 2020; NOT PEER REVIEWED.
27. Tran K, Cimon K, Severn M, et al. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PLoS One* 2012; 7: e35797. 2012/05/09. DOI: 10.1371/journal.pone.0035797.
28. Heinzerling A, Stuckey MJ, Scheuer T, et al. Transmission of COVID-19 to Health Care Personnel During Exposures to a Hospitalized Patient - Solano County, California, February 2020. *MMWR Morb Mortal Wkly Rep* 2020; 69: 472-476. 2020/04/17. DOI: 10.15585/mmwr.mm6915e5.

29. World Health Organization. Infection prevention and control of epidemic and pandemic prone acute respiratory infections in health care. WHO Guidelines. 2014.
30. Thompson KA, Pappachan JV, Bennett AM, et al. Influenza aerosols in UK hospitals during the H1N1 (2009) pandemic--the risk of aerosol generation during medical procedures. PLoS One 2013; 8: e56278. 2013/02/19. DOI: 10.1371/journal.pone.0056278.
31. Chung FF, Lin HL, Liu HE, et al. Aerosol distribution during open suctioning and long-term surveillance of air quality in a respiratory care center within a medical center. Respir Care 2015; 60: 30-37. 2014/10/16. DOI: 10.4187/respcare.03310.
32. Simonds AK, Hanak A, Chatwin M, et al. Evaluation of droplet dispersion during non-invasive ventilation, oxygen therapy, nebuliser treatment and chest physiotherapy in clinical practice: implications for management of pandemic influenza and other airborne infections. Health Technol Assess 2010; 14: 131-172. 2010/10/07. DOI: 10.3310/hta14460-02.
33. Health Protection Scotland. Assessing the evidence base for medical procedures which create a higher risk of respiratory infection transmission from patient to healthcare worker. 12 May 2020 2020.
34. Gaythorpe K, Imai N, Cuomo-Dannenburg G, et al. Report 8: Symptom progression of COVID-19. 11 March 2020 2020. Imperial College London: Imperial College London.
35. Ma S, Zhang J, Zeng M, et al. Epidemiological parameters of coronavirus disease 2019: a pooled analysis of publicly reported individual data of 1155 cases from seven countries. medRxiv 2020; NOT PEER REVIEWED.
36. Li W, Zhang B, Lu J, et al. The characteristics of household transmission of COVID-19. Clin Infect Dis 2020 2020/04/18. DOI: 10.1093/cid/ciaa450.
37. Wang X, Fang J, Zhu Y, et al. Clinical characteristics of non-critically ill patients with novel coronavirus infection (COVID-19) in a Fangcang Hospital. Clin Microbiol Infect 2020 2020/04/07. DOI: 10.1016/j.cmi.2020.03.032.
38. Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ (Clinical research ed) 2020; 368: m606.
39. Wang L, Duan Y, Zhang W, et al. Epidemiologic and Clinical Characteristics of 26 Cases of COVID-19 Arising from Patient-to-Patient Transmission in Liaocheng, China. Clin Epidemiol 2020; 12: 387-391. 2020/04/21. DOI: 10.2147/CLEP.S249903.
40. Zheng Y, Xiong C, Liu Y, et al. Epidemiological and clinical characteristics analysis of COVID-19 in the surrounding areas of Wuhan, Hubei Province in 2020. Pharmacol Res 2020; 157: 104821. 2020/05/04. DOI: 10.1016/j.phrs.2020.104821.
41. Xia XY, Wu J, Liu HL, et al. Epidemiological and initial clinical characteristics of patients with family aggregation of COVID-19. J Clin Virol 2020; 127: 104360. 2020/04/19. DOI: 10.1016/j.jcv.2020.104360.
42. Li Y, Xu S, Du T, et al. Clinical features of 2019 novel coronavirus infection in Beijing. Journal of Thoracic Disease 2020; 12: 2563-2568.

43. Liu L, Lei X, Xiao X, et al. Epidemiological and Clinical Characteristics of Patients With Coronavirus Disease-2019 in Shiyang City, China. *Frontiers in Cellular and Infection Microbiology* 2020; 10.
44. Patel NA. Pediatric COVID-19: Systematic review of the literature. *Am J Otolaryngol* 2020; 41: 102573. 2020/06/13. DOI: 10.1016/j.amjoto.2020.102573.
45. Alsafayan YM, Althunayyan SM, Khan AA, et al. Clinical characteristics of COVID-19 in Saudi Arabia: A national retrospective study. *J Infect Public Health* 2020 2020/06/15. DOI: 10.1016/j.jiph.2020.05.026.
46. Salva EP, Villarama JB, Lopez EB, et al. Epidemiological and clinical characteristics of patients with suspected COVID-19 admitted in Metro Manila, Philippines. *Trop Med Health* 2020; 48: 51. 2020/06/25. DOI: 10.1186/s41182-020-00241-8.
47. Tomlins J, Hamilton F, Gunning S, et al. Clinical features of 95 sequential hospitalised patients with novel coronavirus 2019 disease (COVID-19), the first UK cohort. *J Infect* 2020 2020/05/01. DOI: 10.1016/j.jinf.2020.04.020.
48. Clemency BM, Varughese R, Scheafer DK, et al. Symptom Criteria for COVID-19 Testing of Health Care Workers. *Acad Emerg Med* 2020; 27: 469-474. 2020/05/13. DOI: 10.1111/acem.14009.
49. Chau NVV and al. e. The natural history and transmission potential of asymptomatic SARS-CoV-2 infection. *medRxiv* 2020; PRE-PRINT. DOI: <https://doi.org/10.1101/2020.04.27.20082347>.
50. Paoli D, Pallotti F, Colangelo S, et al. Study of SARS-CoV-2 in semen and urine samples of a volunteer with positive naso-pharyngeal swab. *J Endocrinol Invest* 2020 2020/04/25. DOI: 10.1007/s40618-020-01261-1.
51. Altin F, Cingi C, Uzun T, et al. Olfactory and gustatory abnormalities in COVID-19 cases. *Eur Arch Otorhinolaryngol* 2020 2020/06/25. DOI: 10.1007/s00405-020-06155-9.
52. Noh JY, Yoon JG, Seong H, et al. Asymptomatic infection and atypical manifestations of COVID-19: Comparison of viral shedding duration. *J Infect* 2020 2020/05/24. DOI: 10.1016/j.jinf.2020.05.035.
53. CDC COVID-19 Response Team. Coronavirus diseases 2019 in children - United States, February 12 - April 2, 2020. *Morbidity and Mortality Weekly Report* 2020; 69: 422-426.
54. Tan YP, Tan BY, Pan J, et al. Epidemiologic and clinical characteristics of 10 children with coronavirus disease 2019 in Changsha, China. *J Clin Virol* 2020; 127: 104353. 2020/04/18. DOI: 10.1016/j.jcv.2020.104353.
55. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020; 109: 1088-1095. 2020/03/24. DOI: 10.1111/apa.15270.
56. Chang TH, Wu JL and Chang LY. Clinical characteristics and diagnostic challenges of pediatric COVID-19: A systematic review and meta-analysis. *J Formos Med Assoc* 2020; 119: 982-989. 2020/04/21. DOI: 10.1016/j.jfma.2020.04.007.

57. Zhen-Dong Y, Gao-Jun Z, Run-Ming J, et al. Clinical and transmission dynamics characteristics of 406 children with coronavirus disease 2019 in China: A review. *J Infect* 2020 2020/05/04. DOI: 10.1016/j.jinf.2020.04.030.
58. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 Among Children in China. *Pediatrics* 2020; 145 2020/03/18. DOI: 10.1542/peds.2020-0702.
59. Graham NSN, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes. *medRxiv* 2020; PRE-PRINT. DOI: <https://doi.org/10.1101/2020.05.19.20105460>.
60. Zuin M, Rigatelli G, Zuliani G, et al. Arterial hypertension and risk of death in patients with COVID-19 infection: Systematic review and meta-analysis. *J Infect* 2020 2020/04/14. DOI: 10.1016/j.jinf.2020.03.059.
61. CDC COVID-19 Response Team. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 — United States, February 12–March 28, 2020. *Morbidity and Mortality Weekly Report* 2020; 69.
62. Lian J, Jin X, Hao S, et al. Epidemiological, clinical, and virological characteristics of 465 hospitalized cases of coronavirus disease 2019 (COVID-19) from Zhejiang province in China. *Influenza Other Respir Viruses* 2020 2020/05/13. DOI: 10.1111/irv.12758.
63. Khan MA, Khan N, Mustagir G, et al. Effects of pre-existing morbidities on occurrence of death among COVID-19 disease patients: A systematic review and meta-analysis. *MedRxiv* 2020; PRE-PRINT.
64. Rogado J, Obispo B, Pangua C, et al. Covid-19 transmission, outcome and associated risk factors in cancer patients at the first month of the pandemic in a Spanish hospital in Madrid. *Clin Transl Oncol* 2020 2020/05/26. DOI: 10.1007/s12094-020-02381-z.
65. Field RE, Afzal I, Dixon J, et al. Cohort profile: Preliminary experience of 500 COVID-19 positive cases at a South West London District General Hospital. *medRxiv* 2020; UNPUBLISHED. DOI: <https://doi.org/10.1101/2020.04.28.20075119>.
66. Mannheim J, Gretsch S, Layden JE, et al. Characteristics of Hospitalized Pediatric COVID-19 Cases - Chicago, Illinois, March - April 2020. *J Pediatric Infect Dis Soc* 2020 2020/06/02. DOI: 10.1093/jpids/piaa070.
67. Zhao X. ZB, Li P., Ma C., Gu J., Hou P., Gou Z., Wu H., Bai Y. Incidence, clinical characteristics and prognostic factors of patients with COVID-19: a systematic review and meta-analysis. *medRxiv* 2020.
68. Chu J, Yang N, Wei Y, et al. Clinical characteristics of 54 medical staff with COVID-19: A retrospective study in a single center in Wuhan, China. *J Med Virol* 2020 2020/03/31. DOI: 10.1002/jmv.25793.
69. Tian Y, Rong L, Nian W, et al. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. *Aliment Pharmacol Ther* 2020; 51: 843-851. 2020/03/31. DOI: 10.1111/apt.15731.

70. Lee IC, Huo TI and Huang YH. Gastrointestinal and Liver Manifestations in Patients with COVID-19. *J Chin Med Assoc* 2020 2020/04/04. DOI: 10.1097/JCMA.0000000000000319.
71. Chen Y, Chen L, Deng Q, et al. The Presence of SARS-CoV-2 RNA in Feces of COVID-19 Patients. *J Med Virol* 2020 2020/04/04. DOI: 10.1002/jmv.25825.
72. Zhang R, Ouyang H, Fu L, et al. CT features of SARS-CoV-2 pneumonia according to clinical presentation: a retrospective analysis of 120 consecutive patients from Wuhan city. *Eur Radiol* 2020 2020/04/13. DOI: 10.1007/s00330-020-06854-1.
73. D'Amico F, Baumgart DC, Danese S, et al. Diarrhea during COVID-19 infection: pathogenesis, epidemiology, prevention and management. *Clin Gastroenterol Hepatol* 2020 2020/04/12. DOI: 10.1016/j.cgh.2020.04.001.
74. Liu J, Liao X, Qian S, et al. Community Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, Shenzhen, China, 2020. *Emerging Infectious Diseases* 2020; 26: 17.
75. Cheung KS, Hung IFN, Chan PPY, et al. Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples From a Hong Kong Cohort: Systematic Review and Meta-analysis. *Gastroenterology* 2020 2020/04/07. DOI: 10.1053/j.gastro.2020.03.065.
76. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020 2020/02/29. DOI: 10.1056/NEJMoa2002032.
77. Gao QY, Chen YX and Fang JY. 2019 novel coronavirus infection and gastrointestinal tract. *Journal of digestive diseases* 2020; 25.
78. Yeo C, Kaushal S and Yeo D. Enteric involvement of coronaviruses: is faecal-oral transmission of SARS-CoV-2 possible? *The lancet Gastroenterology & hepatology* 2020; 19.
79. Tang A TZ-d, Wang H-l, Dai Y-x, Li K-f, Liu J-n, et al. . Detection of novel coronavirus by RT-PCR in stool specimen from asymptomatic child, China. . *Emerging Infectious Diseases* 2020; 26.
80. Holshue ML, DeBolt C, Lindquist S, et al. First Case of 2019 Novel Coronavirus in the United States. *N Engl J Med* 2020; 382: 929-936. 2020/02/01. DOI: 10.1056/NEJMoa2001191.
81. Zhang W, Du RH, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect* 2020; 9: 386-389. 2020/02/18. DOI: 10.1080/22221751.2020.1729071.
82. Young Park J. SHM, Un Park K., Young Kim J., Hwa Choi E. First pediatric case of coronavirus disease 2019 in Korea. *Journal of Korean Medical Science* 2020; 35.
83. Zhang T, Cui X, Zhao X, et al. Detectable SARS-CoV-2 viral RNA in feces of three children during recovery period of COVID-19 pneumonia. *J Med Virol* 2020 2020/03/31. DOI: 10.1002/jmv.25795.
84. Xiao F, Tang M, Zheng X, et al. Evidence for Gastrointestinal Infection of SARS-CoV-2. *Gastroenterology* 2020 2020/03/07. DOI: 10.1053/j.gastro.2020.02.055.
85. Nicastri E, D'Abramo A, Faggioni G, et al. Coronavirus disease (COVID-19) in a paucisymptomatic patient: epidemiological and clinical challenge in settings with limited

- community transmission, Italy, February 2020. *Euro Surveill* 2020; 25 2020/03/27. DOI: 10.2807/1560-7917.ES.2020.25.11.2000230.
86. Novazzi F, Cassaniti I, Piralla A, et al. SARS-CoV-2 positivity in rectal swabs implication for possible transmission. *Journal of Global Antimicrobial Resistance* 2020. DOI: <https://doi.org/10.1016/j.jgar.2020.06.011>.
87. Wong MC, Huang J, Lai C, et al. Detection of SARS-CoV-2 RNA in fecal specimens of patients with confirmed COVID-19: A meta-analysis. *J Infect* 2020 2020/06/15. DOI: 10.1016/j.jinf.2020.06.012.
88. Santos VS, Gurgel RQ, Cuevas LE, et al. Prolonged fecal shedding of SARS-CoV-2 in pediatric patients. A quantitative evidence synthesis. *J Pediatr Gastroenterol Nutr* 2020 2020/05/27. DOI: 10.1097/MPG.0000000000002798.
89. Li J, Feng J, Liu TH, et al. An infant with a mild SARS-CoV-2 infection detected only by anal swabs: a case report. *Braz J Infect Dis* 2020 2020/05/12. DOI: 10.1016/j.bjid.2020.04.009.
90. Xu Y, Li X, Zhu B, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med* 2020; 26: 502-505. 2020/04/15. DOI: 10.1038/s41591-020-0817-4.
91. Park SK, Lee CW, Park DI, et al. Detection of SARS-CoV-2 in Fecal Samples from Patients with Asymptomatic and Mild COVID-19 in Korea. *Clin Gastroenterol Hepatol* 2020 2020/06/14. DOI: 10.1016/j.cgh.2020.06.005.
92. Wolfel R, Corman V.M., Guggemos W., Seilmaier M., Zange S., Muller M.A., Niemeyer D., Jones Kelly T.C., Vollmar P., Rothe C., Hoelscher M., Bleicker T., Brunink S., Schneider J., Ethmann R., Zwirgmaier K., Drosten C., Wendtner C. Virological assessment of hospitalized cases of coronavirus disease 2019. *medRxiv* 2020.
93. Xiao F, Sun J, Xu Y, et al. Infectious SARS-CoV-2 in Feces of Patient with Severe COVID-19. *Emerg Infect Dis* 2020; 26 2020/05/19. DOI: 10.3201/eid2608.200681.
94. van Kampen JJA and al. e. Shedding of infectious virus in hospitalised patients with coronavirus disease-2019 (COVID-19): duration and key determinants. *medRxiv* 2020; PREPRINT. DOI: <https://doi.org/10.1101/2020.06.08.20125310>.
95. Chan JFW, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *The Lancet* 2020; 395: 514-523.
96. Chang L, Zhao L, Gong H, et al. Severe acute respiratory syndrome coronavirus 2 RNA detected in blood donations. *Emerging infectious diseases* 2020; 26.
97. Peng L, Liu J, Xu W, et al. 2019 novel coronavirus can be detected in urine, blood, anal swabs and oropharyngeal swabs samples. *medRxiv* 2020; NOT PEER REVIEWED.
98. Han MS, Seong MW, Kim N, et al. Viral RNA Load in Mildly Symptomatic and Asymptomatic Children with COVID-19, Seoul. *Emerg Infect Dis* 2020; 26 2020/06/05. DOI: 10.3201/eid2610.202449.

99. Kim JM, Kim HM, Lee EJ, et al. Detection and Isolation of SARS-CoV-2 in Serum, Urine, and Stool Specimens of COVID-19 Patients from the Republic of Korea. *Osong Public Health Res Perspect* 2020; 11: 112-117. 2020/06/13. DOI: 10.24171/j.phrp.2020.11.3.02.
100. Qiu L, Liu X, Xiao M, et al. SARS-CoV-2 is not detectable in the vaginal fluid of women with severe COVID-19 infection. *Clin Infect Dis* 2020 2020/04/03. DOI: 10.1093/cid/ciaa375.
101. Song C, Wang Y, Li W, et al. Absence of 2019 Novel Coronavirus in Semen and Testes of COVID-19 Patients. *Biol Reprod* 2020 2020/04/17. DOI: 10.1093/biolre/ioaa050.
102. Zhang S, Wang X, Zhang H, et al. The absence of coronavirus in expressed prostatic secretion in COVID-19 patients in Wuhan city. *Reprod Toxicol* 2020; 96: 90-94. 2020/06/14. DOI: 10.1016/j.reprotox.2020.06.006.
103. Li D, Jin M, Bao P, et al. Clinical Characteristics and Results of Semen Tests Among Men With Coronavirus Disease 2019. *JAMA Netw Open* 2020; 3: e208292. 2020/05/08. DOI: 10.1001/jamanetworkopen.2020.8292.
104. Pan F, Xiao X, Guo J, et al. No evidence of severe acute respiratory syndrome-coronavirus 2 in semen of males recovering from coronavirus disease 2019. *Fertil Steril* 2020; 113: 1135-1139. 2020/06/03. DOI: 10.1016/j.fertnstert.2020.04.024.
105. Holtmann N, Edimiris P, Andree M, et al. Assessment of SARS-CoV-2 in human semen-a cohort study. *Fertil Steril* 2020 2020/07/12. DOI: 10.1016/j.fertnstert.2020.05.028.
106. Sun J, Zhu A, Li H, et al. Isolation of Infectious SARS-CoV-2 from Urine of a COVID-19 Patient. *Emerg Microbes Infect* 2020: 1-8. 2020/04/29. DOI: 10.1080/22221751.2020.1760144.
107. Ngaserin SH, Koh FH, Ong BC, et al. COVID-19 not detected in peritoneal fluid: a case of laparoscopic appendicectomy for acute appendicitis in a COVID-19-infected patient. *Langenbecks Arch Surg* 2020; 405: 353-355. 2020/05/10. DOI: 10.1007/s00423-020-01891-2.
108. Wu P, Duan F, Luo C, et al. Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol* 2020 2020/04/02. DOI: 10.1001/jamaophthalmol.2020.1291.
109. Zhang X, Chen X, Chen L, et al. The evidence of SARS-CoV-2 infection on ocular surface. *Ocul Surf* 2020 2020/04/15. DOI: 10.1016/j.jtos.2020.03.010.
110. Salducci M and La Torre G. COVID-19 emergency in the cruise's ship: a case report of conjunctivitis. *Clin Ter* 2020; 171: e189-e191. 2020/04/24. DOI: 10.7417/CT.2020.2212.
111. Karimi S, Arabi A, Shahraki T, et al. Detection of severe acute respiratory syndrome Coronavirus-2 in the tears of patients with Coronavirus disease 2019. *Eye (Lond)* 2020 2020/05/20. DOI: 10.1038/s41433-020-0965-2.
112. Liang L and Wu P. There may be virus in conjunctival secretion of patients with COVID-19. *Acta Ophthalmol* 2020; 98: 223. 2020/03/20. DOI: 10.1111/aos.14413.
113. Valente P, Iarossi G, Federici M, et al. Ocular manifestations and viral shedding in tears of pediatric patients with coronavirus disease 2019: a preliminary report. *J AAPOS* 2020 2020/06/13. DOI: 10.1016/j.jaapos.2020.05.002.

114. Hu Y, Chen T, Liu M, et al. Positive detection of SARS-CoV-2 combined HSV1 and HHV6B virus nucleic acid in tear and conjunctival secretions of a non-conjunctivitis COVID-19 patient with obstruction of common lacrimal duct. *Acta Ophthalmol* 2020 2020/05/15. DOI: 10.1111/aos.14456.
115. Fang Z, Zhang Y, Hang C, et al. Comparisons of viral shedding time of SARS-CoV-2 of different samples in ICU and non-ICU patients. *J Infect* 2020; 81: 147-178. 2020/03/27. DOI: 10.1016/j.jinf.2020.03.013.
116. Li JPO, Lam DSC, Chen Y, et al. Novel Coronavirus disease 2019 (COVID-19): The importance of recognising possible early ocular manifestation and using protective eyewear. *The British journal of ophthalmology* 2020; 104: 297-298. Editorial.
117. Lu CW, Liu XF and Jia ZF. 2019-nCoV transmission through the ocular surface must not be ignored. *The Lancet* 2020; 395: e39. Letter.
118. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *The Lancet* 2020.
119. Yu N, Li W, Kang Q, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *Lancet Infect Dis* 2020 2020/03/30. DOI: 10.1016/S1473-3099(20)30176-6.
120. Yang P, Wang X, Liu P, et al. Clinical characteristics and risk assessment of newborns born to mothers with COVID-19. *J Clin Virol* 2020; 127: 104356. 2020/04/18. DOI: 10.1016/j.jcv.2020.104356.
121. Chen Y, Peng H, Wang L, et al. Infants Born to Mothers With a New Coronavirus (COVID-19). *Front Pediatr* 2020; 8: 104. 2020/04/09. DOI: 10.3389/fped.2020.00104.
122. Lu D, Sang L, Du S, et al. Asymptomatic COVID-19 infection in late pregnancy indicated no vertical transmission. *J Med Virol* 2020 2020/04/25. DOI: 10.1002/jmv.25927.
123. Kuhrt K, McMicking J, Nanda S, et al. Placental abruption in a twin pregnancy at 32 weeks' gestation complicated by COVID-19, without vertical transmission to the babies. *Am J Obstet Gynecol MFM* 2020: 100135. 2020/05/12. DOI: 10.1016/j.ajogmf.2020.100135.
124. Lyra J, Valente R, Rosario M, et al. Cesarean Section in a Pregnant Woman with COVID-19: First Case in Portugal. *Acta Med Port* 2020; 33: 429-431. 2020/05/01. DOI: 10.20344/amp.13883.
125. Sun M, Xu G, Yang Y, et al. Evidence of mother-to-newborn infection with COVID-19. *Br J Anaesth* 2020 2020/05/11. DOI: 10.1016/j.bja.2020.04.066.
126. Prabhu M, Cagino K, Matthews KC, et al. Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in New York City: A prospective cohort study. *BJOG* 2020 2020/07/08. DOI: 10.1111/1471-0528.16403.
127. Khan S, Peng L, Siddique R, et al. Impact of COVID-19 infection on pregnancy outcomes and the risk of maternal-to-neonatal intrapartum transmission of COVID-19 during natural birth. *Infect Control Hosp Epidemiol* 2020: 1-3. 2020/04/14. DOI: 10.1017/ice.2020.84.

128. Dong L, Tian J, He S, et al. Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn. *JAMA* 2020 2020/03/28. DOI: 10.1001/jama.2020.4621.
129. Xiong X, Wei H, Zhang Z, et al. Vaginal Delivery Report of a Healthy Neonate Born to a Convalescent Mother with COVID-19. *J Med Virol* 2020 2020/04/11. DOI: 10.1002/jmv.25857.
130. Liu W, Wang J, Li W, et al. Clinical characteristics of 19 neonates born to mothers with COVID-19. *Front Med* 2020 2020/04/15. DOI: 10.1007/s11684-020-0772-y.
131. Cao D, Yin H, Chen J, et al. Clinical analysis of ten pregnant women with COVID-19 in Wuhan, China: A retrospective study. *Int J Infect Dis* 2020; 95: 294-300. 2020/04/27. DOI: 10.1016/j.ijid.2020.04.047.
132. Penfield CA, Brubaker SG, Limaye MA, et al. Detection of SARS-COV-2 in Placental and Fetal Membrane Samples. *Am J Obstet Gynecol MFM* 2020: 100133. 2020/05/12. DOI: 10.1016/j.ajogmf.2020.100133.
133. De Socio GV, Malincarne L, Arena S, et al. Delivery in Asymptomatic Italian Woman with SARS-CoV-2 Infection. *Mediterr J Hematol Infect Dis* 2020; 12: e2020033. 2020/05/13. DOI: 10.4084/MJHID.2020.033.
134. Perrone S, Deolmi M, Giordano M, et al. Report of a series of healthy term newborns from convalescent mothers with COVID-19. *Acta Biomed* 2020; 91: 251-255. 2020/05/19. DOI: 10.23750/abm.v91i2.9743.
135. Parazzini F, Bortolus R, Mauri PA, et al. Delivery in pregnant women infected with SARS-CoV-2: A fast review. *Int J Gynaecol Obstet* 2020 2020/04/10. DOI: 10.1002/ijgo.13166.
136. Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, et al. Vertical Transmission of Coronavirus Disease 19 (COVID-19) from Infected Pregnant Mothers to Neonates: A Review. *Fetal Pediatr Pathol* 2020: 1-5. 2020/04/03. DOI: 10.1080/15513815.2020.1747120.
137. Di Mascio D, Khalil A, Saccone G, et al. Outcome of Coronavirus spectrum infections (SARS, MERS, COVID 1 -19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM* 2020: 100107. 2020/04/16. DOI: 10.1016/j.ajogmf.2020.100107.
138. Cheruiyot I, Henry BM and Lippi G. Is there evidence of intra-uterine vertical transmission potential of COVID-19 infection in samples tested by quantitative RT-PCR? *Eur J Obstet Gynecol Reprod Biol* 2020 2020/04/28. DOI: 10.1016/j.ejogrb.2020.04.034.
139. Smith V, Seo D, Warty R, et al. Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review. *PLoS One* 2020; 15: e0234187. 2020/06/05. DOI: 10.1371/journal.pone.0234187.
140. Huntley BJF, Huntley ES, Di Mascio D, et al. Rates of Maternal and Perinatal Mortality and Vertical Transmission in Pregnancies Complicated by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Co-V-2) Infection: A Systematic Review. *Obstet Gynecol* 2020 2020/06/10. DOI: 10.1097/AOG.0000000000004010.
141. Zamaniyan M, Ebadi A, Aghajanpoor Mir S, et al. Preterm delivery in pregnant woman with critical COVID-19 pneumonia and vertical transmission. *Prenat Diagn* 2020 2020/04/19. DOI: 10.1002/pd.5713.

142. Patane L, Morotti D, Giunta MR, et al. Vertical transmission of COVID-19: SARS-CoV-2 RNA on the fetal side of the placenta in pregnancies with COVID-19 positive mothers and neonates at birth. *Am J Obstet Gynecol MFM* 2020: 100145. 2020/05/20. DOI: 10.1016/j.ajogmf.2020.100145.
143. Zeng L, Xia S, Yuan W, et al. Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China. *JAMA Pediatr* 2020 2020/03/28. DOI: 10.1001/jamapediatrics.2020.0878.
144. Alzamora MC, Paredes T, Caceres D, et al. Severe COVID-19 during Pregnancy and Possible Vertical Transmission. *Am J Perinatol* 2020 2020/04/19. DOI: 10.1055/s-0040-1710050.
145. Khan S, Jun L, Nawsherwan, et al. Association of COVID-19 with pregnancy outcomes in health-care workers and general women. *Clin Microbiol Infect* 2020 2020/04/12. DOI: 10.1016/j.cmi.2020.03.034.
146. Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ* 2020; 369: m2107. 2020/06/10. DOI: 10.1136/bmj.m2107.
147. Sisman J, Jaleel MA, Moreno W, et al. Intrauterine Transmission of Sars-Cov-2 Infection in a Preterm Infant. *Pediatr Infect Dis J* 2020 2020/07/14. DOI: 10.1097/INF.0000000000002815.
148. Wang S, Guo L, Chen L, et al. A case report of neonatal COVID-19 infection in China. *Clin Infect Dis* 2020 2020/03/13. DOI: 10.1093/cid/ciaa225.
149. Nie R and al. e. Clinical features and the maternal and neonatal outcomes of pregnant women with coronavirus disease 2019. *medRxiv* 2020; NOT PEER REVIEWED.
150. Hu X, Gao J, Luo X, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vertical Transmission in Neonates Born to Mothers With Coronavirus Disease 2019 (COVID-19) Pneumonia. *Obstet Gynecol* 2020 2020/04/26. DOI: 10.1097/AOG.0000000000003926.
151. Zeng H, Xu C, Fan J, et al. Antibodies in Infants Born to Mothers With COVID-19 Pneumonia. *JAMA* 2020 2020/03/28. DOI: 10.1001/jama.2020.4861.
152. Gao J, Li W, Hu X, et al. Disappearance of SARS-CoV-2 Antibodies in Infants Born to Women with COVID-19, Wuhan, China. *Emerg Infect Dis* 2020; 26 2020/07/06. DOI: 10.3201/eid2610.202328.
153. Dashraath P, Jing Lin Jeslyn W, Mei Xian Karen L, et al. Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy. *Am J Obstet Gynecol* 2020 2020/03/29. DOI: 10.1016/j.ajog.2020.03.021.
154. Wu Y, Liu C, Dong L, et al. Viral shedding of COVID-19 in pregnant women. *SSRN* 2020; PREPRINT.
155. Gross R, Conzelmann C, Muller JA, et al. Detection of SARS-CoV-2 in human breastmilk. *Lancet* 2020; 395: 1757-1758. 2020/05/25. DOI: 10.1016/S0140-6736(20)31181-8.
156. Bastug A, Hanifehnezhad A, Tayman C, et al. Virolactia in an Asymptomatic Mother with COVID-19. *Breastfeed Med* 2020 2020/07/03. DOI: 10.1089/bfm.2020.0161.

157. World Health Organization. Breastfeeding and COVID-19. 23 June 2020 2020. Geneva: World Health Organization.
158. Ferrazzi E, Frigerio L, Savasi V, et al. Vaginal delivery in SARS-CoV-2 infected pregnant women in Northern Italy: a retrospective analysis. *BJOG* 2020 2020/04/28. DOI: 10.1111/1471-0528.16278.
159. Qiu H, Wu J, Hong L, et al. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis* 2020 2020/03/30. DOI: 10.1016/S1473-3099(20)30198-5.
160. Danis K, Epaulard O, Benet T, et al. Cluster of coronavirus disease 2019 (Covid-19) in the French Alps, 2020. *Clin Infect Dis* 2020 2020/04/12. DOI: 10.1093/cid/ciaa424.
161. Kan MJ, Grant LMC, Muna MA, et al. Fever without a source in a young infant due to SARS-CoV-2. *J Pediatric Infect Dis Soc* 2020 2020/04/23. DOI: 10.1093/jpids/piaa044.
162. Mao ZQ, Wan R, He LY, et al. The enlightenment from two cases of asymptomatic infection with SARS-CoV-2: is it safe after 14 days of isolation? *Int J Infect Dis* 2020 2020/04/07. DOI: 10.1016/j.ijid.2020.03.041.
163. Scalinci SZ and Trovato Battagliola E. Conjunctivitis can be the only presenting sign and symptom of COVID-19. *IDCases* 2020; 20: e00774. 2020/05/07. DOI: 10.1016/j.idcr.2020.e00774.
164. Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet* 2020; 395: 1771-1778. 2020/05/16. DOI: 10.1016/S0140-6736(20)31103-X.
165. Whittaker E, Bamford A, Kenny J, et al. Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. *JAMA* 2020 2020/06/09. DOI: 10.1001/jama.2020.10369.
166. Bataille V, Visconti A, Rossi N, et al. Diagnostic value of skin manifestations of SARS-CoV-2 infection. *medRxiv* 2020; PREPRINT. DOI: <https://doi.org/10.1101/2020.07.10.20150656>.
167. Hormati A. SA, Afifian M., Khodadust F., Ahmadpour S. Can COVID-19 present unusual GI symptoms? *Journal of Microbiology, Immunology and Infection* 2020; In press, Journal Pre-proof.
168. Tay HS and Harwood R. Atypical presentation of COVID-19 in a frail older person. *Age Ageing* 2020 2020/04/22. DOI: 10.1093/ageing/afaa068.
169. Spiteri G, Fielding J, Diercke M, et al. First cases of coronavirus disease 2019 (COVID-19) in the WHO European Region, 24 January to 21 February 2020. *Euro Surveill* 2020; 25 2020/03/12. DOI: 10.2807/1560-7917.ES.2020.25.9.2000178.
170. Jiang X, Luo M, Zou Z, et al. Asymptomatic SARS-CoV-2 infected case with viral detection positive in stool but negative in nasopharyngeal samples lasts for 42 days. *J Med Virol* 2020 2020/04/25. DOI: 10.1002/jmv.25941.

171. Wan R, Mao ZQ, He LY, et al. Evidence from two cases of asymptomatic infection with SARS-CoV-2: Are 14 days of isolation sufficient? *Int J Infect Dis* 2020; 95: 174-175. 2020/04/07. DOI: 10.1016/j.ijid.2020.03.041.
172. Liu Z, Chu R, Gong L, et al. The assessment of transmission efficiency and latent infection period on asymptomatic carriers of SARS-CoV-2 infection. *Int J Infect Dis* 2020 2020/06/17. DOI: 10.1016/j.ijid.2020.06.036.
173. Ochiai D, Kasuga Y, Iida M, et al. Universal screening for SARS-CoV-2 in asymptomatic obstetric patients in Tokyo, Japan. *Int J Gynaecol Obstet* 2020 2020/06/05. DOI: 10.1002/ijgo.13252.
174. Bai Y, Yao L, Wei T, et al. Presumed Asymptomatic Carrier Transmission of COVID-19. *Jama* 2020; 21.
175. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. *The New England journal of medicine* 2020; 30. Letter.
176. Hu Z, Song C, Xu C, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Sci China Life Sci* 2020; 63: 706-711. 2020/03/09. DOI: 10.1007/s11427-020-1661-4.
177. Zhou R, Li F, Chen F, et al. Viral dynamics in asymptomatic patients with COVID-19. *Int J Infect Dis* 2020; 96: 288-290. 2020/05/22. DOI: 10.1016/j.ijid.2020.05.030.
178. Kong W, Wang Y, Hu J, et al. Comparison of clinical and epidemiological characteristics of asymptomatic and symptomatic SARS-CoV-2 infection: A multi-center study in Sichuan Province, China. *Travel Med Infect Dis* 2020: 101754. 2020/06/04. DOI: 10.1016/j.tmaid.2020.101754.
179. Xiao T and al. e. Early viral clearance and antibody kinetics of COVID-19 among asymptomatic carriers. . *MedRxiv* 2020; NOT PEER REVIEWED.
180. Lin J, Duan J, Tan T, et al. The isolation period should be longer: Lesson from a child infected with SARS-CoV-2 in Chongqing, China. *Pediatr Pulmonol* 2020; 55: E6-E9. 2020/04/04. DOI: 10.1002/ppul.24763.
181. Diercks GR, Park BJ, Myers LB, et al. Asymptomatic COVID-19 infection in a child with nasal foreign body. *Int J Pediatr Otorhinolaryngol* 2020; 135: 110092. 2020/06/02. DOI: 10.1016/j.ijporl.2020.110092.
182. Hijnen D, Marzano AV, Eyerich K, et al. SARS-CoV-2 Transmission from Presymptomatic Meeting Attendee, Germany. *Emerg Infect Dis* 2020; 26 2020/05/12. DOI: 10.3201/eid2608.201235.
183. Wei W.E. LZ, Chiew C.J., Yong S.E., Toh M.T., Lee V.J. Presymptomatic transmission of SARS-CoV-2 - Singapore, January 23-March 16, 2020. *Morbidity and Mortality Weekly Report* 2020; 69 - Early Release.
184. Tong ZD, Tang A, Li KF, et al. Potential Presymptomatic Transmission of SARS-CoV-2, Zhejiang Province, China, 2020. *Emerging infectious diseases* 2020; 26.

185. Huang L, Zhang X, Zhang X, et al. Rapid asymptomatic transmission of COVID-19 during the incubation period demonstrating strong infectivity in a cluster of youngsters aged 16-23 years outside Wuhan and characteristics of young patients with COVID-19: A prospective contact-tracing study. *J Infect* 2020 2020/04/14. DOI: 10.1016/j.jinf.2020.03.006.
186. Gao Y, Shi C, Chen Y, et al. A cluster of the Corona Virus Disease 2019 caused by incubation period transmission in Wuxi, China. *J Infect* 2020 2020/04/14. DOI: 10.1016/j.jinf.2020.03.042.
187. Bohmer MM, Buchholz U, Corman VM, et al. Investigation of a COVID-19 outbreak in Germany resulting from a single travel-associated primary case: a case series. *Lancet Infect Dis* 2020 2020/05/19. DOI: 10.1016/S1473-3099(20)30314-5.
188. Chen M, Fan P, Liu Z, et al. A SARS-CoV-2 familial cluster infection reveals asymptomatic transmission to children. *J Infect Public Health* 2020; 13: 883-886. 2020/06/09. DOI: 10.1016/j.jiph.2020.05.018.
189. Sang H, Cui Y, Lai X, et al. A familial cluster of coronavirus disease 2019 (COVID-19) caused by one family member during his asymptomatic incubation period. *J Public Health (Oxf)* 2020 2020/07/11. DOI: 10.1093/pubmed/fdaa098.
190. Lai X, Wang M, Qin C, et al. Coronavirus Disease 2019 (COVID-2019) Infection Among Health Care Workers and Implications for Prevention Measures in a Tertiary Hospital in Wuhan, China. *JAMA Netw Open* 2020; 3: e209666. 2020/05/22. DOI: 10.1001/jamanetworkopen.2020.9666.
191. Kluytmans-van den Bergh M.F.Q. BAGM, Pas S.D., Bentvelsen R.G., van den Bijllaardt W., van Oudheusden A.J.G., van Rijen M.M.L., Verweij J.J., Koopmans M.P.G., Kluytmans J.A.J.W. . SARS-CoV-2 infection in 86 healthcare workers in two Dutch hospitals in March 2020. *medRxiv* 2020; NOT PEER REVIEWED.
192. Wang X, Zhou Q, He Y, et al. Nosocomial outbreak of COVID-19 pneumonia in Wuhan, China. *Eur Respir J* 2020; 55 2020/05/06. DOI: 10.1183/13993003.00544-2020.
193. Schwierzeck V, König JC, Kuhn J, et al. First reported nosocomial outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a pediatric dialysis unit. *Clin Infect Dis* 2020 2020/04/28. DOI: 10.1093/cid/ciaa491.
194. Wei XS, Wang XR, Zhang JC, et al. A cluster of health care workers with COVID-19 pneumonia caused by SARS-CoV-2. *J Microbiol Immunol Infect* 2020 2020/05/04. DOI: 10.1016/j.jmii.2020.04.013.
195. Dantes RB, Jones TT and Neujahr DC. Delayed Recognition of Community Transmission of COVID-19 Resulting in Healthcare Worker Infections. *Infect Control Hosp Epidemiol* 2020: 1-6. 2020/06/11. DOI: 10.1017/ice.2020.285.
196. Rickman HM, Rampling T, Shaw K, et al. Nosocomial transmission of COVID-19: a retrospective study of 66 hospital-acquired cases in a London teaching hospital. *Clin Infect Dis* 2020 2020/06/21. DOI: 10.1093/cid/ciaa816.
197. Asad H, Johnston C, Blyth I, et al. Health care workers and patients as Trojan horses: a COVID19 ward outbreak. *Infection Prevention in Practice* 2020; 2.

198. Hunter E, Price DA, Murphy E, et al. First experience of COVID-19 screening of health-care workers in England. *Lancet* 2020; 395: e77-e78. 2020/04/26. DOI: 10.1016/S0140-6736(20)30970-3.
199. Folgueira MD and al. e. SARS-CoV-2 infection in health care workers in a large public hospital in Madrid, Spain, during March 2020. . *MedRxiv* 2020; NOT PEER REVIEWED.
200. Sikkema RSea. COVID-19 in healthcare workers in three hospitals in the South of the Netherlands, March 2020. *medRxiv* 2020; UNPUBLISHED. DOI: <https://doi.org/10.1101/2020.04.26.20079418>.
201. Safdar N, Moreno GK, Braun KM, et al. Determining the source of transmission of SARS-CoV-2 infection in a healthcare worker. *medRxiv* 2020; PRE-PRINT. DOI: <https://doi.org/10.1101/2020.04.27.20077016>.
202. Rivett L, Sridhar S, Sparkes D, et al. Screening of healthcare workers for SARS-CoV-2 highlights the role of asymptomatic carriage in COVID-19 transmission. *Elife* 2020; 9 2020/05/12. DOI: 10.7554/eLife.58728.
203. Treibel TA, Manisty C, Burton M, et al. COVID-19: PCR screening of asymptomatic health-care workers at London hospital. *The Lancet* 2020. DOI: [https://doi.org/10.1016/S0140-6736\(20\)31100-4](https://doi.org/10.1016/S0140-6736(20)31100-4).
204. Patel MC, Chaisson LH, Borgetti S, et al. Asymptomatic SARS-CoV-2 infection and COVID-19 mortality during an outbreak investigation in a skilled nursing facility. *Clin Infect Dis* 2020 2020/06/18. DOI: 10.1093/cid/ciaa763.
205. Canova V, Lederer Schlapfer H, Piso RJ, et al. Transmission risk of SARS-CoV-2 to healthcare workers -observational results of a primary care hospital contact tracing. *Swiss Med Wkly* 2020; 150: w20257. 2020/04/26. DOI: 10.4414/smw.2020.20257.
206. Wendt R, Nagel S, Nickel O, et al. Comprehensive investigation of an in-hospital transmission cluster of a symptomatic SARS-CoV-2-positive physician among patients and healthcare workers in Germany. *Infect Control Hosp Epidemiol* 2020; 1-3. 2020/06/04. DOI: 10.1017/ice.2020.268.
207. Ng K, Poon BH, Kiat Puar TH, et al. COVID-19 and the Risk to Health Care Workers: A Case Report. *Ann Intern Med* 2020; 172: 766-767. 2020/03/17. DOI: 10.7326/L20-0175.
208. Boldog P, Tekeli T, Vizi Z, et al. Risk assessment of novel coronavirus COVID-19 outbreaks outside China. *Journal of Clinical Medicine* 2020; 9 (2) (no pagination).
209. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *The New England journal of medicine* 2020; 29.
210. Lauer SA, Grantz KH, Bi Q, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med* 2020 2020/03/10. DOI: 10.7326/M20-0504.
211. World Health Organization. Report of the WHO-China Joint Commission on Coronavirus disease 2019. 2020. World Health Organization.

212. Sohrabi C, Alsafi Z, O'Neill N, et al. World Health Organization declares Global Emergency: A review of the 2019 Novel Coronavirus (COVID-19). *International Journal Of Surgery* 2020; 26: 26. Review.
213. Tian S, Hu N, Lou J, et al. Characteristics of COVID-19 infection in Beijing. *Journal of Infection* 2020; 26: 26.
214. Backer JA, Klinkenberg D and Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20-28 January 2020. *Euro Surveill* 2020; 25 2020/02/13. DOI: 10.2807/1560-7917.ES.2020.25.5.2000062.
215. Fan J, Liu X, Pan W, et al. Epidemiology of 2019 Novel Coronavirus Disease-19 in Gansu Province, China, 2020. *Emerg Infect Dis* 2020; 26 2020/03/14. DOI: 10.3201/eid2606.200251.
216. Jiang X, Rayner S and Luo MH. Does SARS-CoV-2 has a longer incubation period than SARS and MERS? *J Med Virol* 2020; 92: 476-478. 2020/02/15. DOI: 10.1002/jmv.25708.
217. COVID-19 National Emergency Response Center EaCMT, Korea Centers for Disease Control and Prevention,. Early epidemiological and clinical characteristics of 28 cases of coronavirus disease in South Korea. *Osong Public Health Research Perspective* 2020; 11: 8-14.
218. Zhang J, Litvinova M, Wang W, et al. Evolving epidemiology and transmission dynamics of coronavirus disease 2019 outside Hubei province, China: a descriptive and modelling study. *Lancet Infect Dis* 2020 2020/04/06. DOI: 10.1016/S1473-3099(20)30230-9.
219. Tindale LC, Stockdale JE, Coombe M, et al. Evidence for transmission of COVID-19 prior to symptom onset. *Elife* 2020; 9 2020/06/23. DOI: 10.7554/eLife.57149.
220. Zhao C, Xu Y, Zhang X, et al. Public health initiatives from hospitalized patients with COVID-19, China. *J Infect Public Health* 2020 2020/06/28. DOI: 10.1016/j.jiph.2020.06.013.
221. Yang L, Dai J, Zhao J, et al. Estimation of incubation period and serial interval of COVID-19: analysis of 178 cases and 131 transmission chains in Hubei province, China. *Epidemiol Infect* 2020; 148: e117. 2020/07/01. DOI: 10.1017/S0950268820001338.
222. Deng SQ and Peng HJ. Characteristics of and public health responses to the coronavirus disease 2019 outbreak in China. *Journal of Clinical Medicine* 2020; 9 (2) (no pagination). Review.
223. Lillie PJ, Samson A, Li A, et al. Novel coronavirus disease (Covid-19): the first two patients in the UK with person to person transmission. *Journal of Infection* 2020; 28: 28. Letter.
224. Pung R, Chiew CJ, Young BE, et al. Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures. *Lancet* 2020; 395: 1039-1046. 2020/03/21. DOI: 10.1016/S0140-6736(20)30528-6.
225. Xiao Z, Xie X, Guo W, et al. Examining the incubation period distributions of COVID-19 on Chinese patients with different travel histories. *J Infect Dev Ctries* 2020; 14: 323-327. 2020/05/08. DOI: 10.3855/jidc.12718.
226. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020 2020/03/15. DOI: 10.1016/S0140-6736(20)30566-3.

227. Chen X, Hu W, Ling J, et al. Hypertension and diabetes delay the viral clearance in COVID-19 patients. medRxiv 2020; NOT PEER REVIEWED.
228. To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis* 2020 2020/03/28. DOI: 10.1016/S1473-3099(20)30196-1.
229. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med* 2020 2020/04/17. DOI: 10.1038/s41591-020-0869-5.
230. Kim NJ, Choe PG, Park SJ, et al. A cluster of tertiary transmissions of 2019 novel coronavirus (SARS-CoV-2) in the community from infectors with common cold symptoms. *Korean J Intern Med* 2020 2020/06/09. DOI: 10.3904/kjim.2020.122.
231. Xiao AT, Tong YX, Gao C, et al. Dynamic profile of RT-PCR findings from 301 COVID-19 patients in Wuhan, China: A descriptive study. *J Clin Virol* 2020; 127: 104346. 2020/05/04. DOI: 10.1016/j.jcv.2020.104346.
232. Wang K, Zhang X, Sun J, et al. Differences of SARS-CoV-2 Shedding Duration in Sputum and Nasopharyngeal Swab Specimens among Adult Inpatients with COVID-19. *Chest* 2020 2020/06/23. DOI: 10.1016/j.chest.2020.06.015.
233. Saurabh S, Kumar R, Gupta MK, et al. Prolonged persistence of SARS-CoV-2 in the upper respiratory tract of asymptomatic infected individuals. *QJM* 2020 2020/07/02. DOI: 10.1093/qjmed/hcaa212.
234. Gombar S, Chang M, Hogan CA, et al. Persistent detection of SARS-CoV-2 RNA in patients and healthcare workers with COVID-19. *J Clin Virol* 2020; 129: 104477. 2020/06/09. DOI: 10.1016/j.jcv.2020.104477.
235. Deng W, Guang TW, Yang M, et al. Positive results for patients with COVID-19 discharged from hospital in Chongqing, China. *BMC Infect Dis* 2020; 20: 429. 2020/06/21. DOI: 10.1186/s12879-020-05151-y.
236. Li W, Su YY, Zhi SS, et al. Viral shedding dynamics in asymptomatic and mildly symptomatic patients infected with SARS-CoV-2. *Clin Microbiol Infect* 2020 2020/07/13. DOI: 10.1016/j.cmi.2020.07.008.
237. L'Hullier AG, Torriani G, Pigny F, et al. Culture-compentent SARS-CoV-2 in nasopharynx of symptomatic neonates, children, and adolescents. *Emerging Infectious Diseases* 2020; 26.
238. Xu K, Chen Y, Yuan J, et al. Factors associated with prolonged viral RNA shedding in patients with COVID-19. *Clin Infect Dis* 2020 2020/04/10. DOI: 10.1093/cid/ciaa351.
239. Lan L, Xu D, Ye G, et al. Positive RT-PCR Test Results in Patients Recovered From COVID-19. *JAMA* 2020 2020/02/28. DOI: 10.1001/jama.2020.2783.
240. Song R, Han B, Song M, et al. Clinical and epidemiological features of COVID-19 family clusters in Beijing, China. *J Infect* 2020 2020/04/27. DOI: 10.1016/j.jinf.2020.04.018.

241. Su JW, Wu WR, Lang GJ, et al. Transmission risk of patients with COVID-19 meeting discharge criteria should be interpreted with caution. *J Zhejiang Univ Sci B* 2020; 21: 408-410. 2020/05/20. DOI: 10.1631/jzus.B2000117.
242. Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. *N Engl J Med* 2020 2020/04/25. DOI: 10.1056/NEJMoa2008457.
243. Kim GU, Kim MJ, Ra SH, et al. Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19. *Clin Microbiol Infect* 2020 2020/05/04. DOI: 10.1016/j.cmi.2020.04.040.
244. Yang R, Gui X and Xiong Y. Patients with respiratory symptoms are at greater risk of COVID-19 transmission. *Respir Med* 2020; 165: 105935. 2020/04/21. DOI: 10.1016/j.rmed.2020.105935.
245. ECDC. Guidance for discharge and ending isolation in the context of widespread community transmission of COVID-19 - first update (8 April 2020). 8 April 2020 2020. ECDC.
246. Health Protection Scotland. Guidance for stepdown of infection control precautions and discharging COVID-19 patients from hospital to residential settings, Version 1.0. 11 April 2020 2020.
247. Public Health England. Guidance for stepdown of infection control precautions and discharging COVID-19 patients (18 April 2020). 18 April 2020.
248. Department of Health England and Health Protection Agency. Pandemic (H1N1) 2009 Influenza. Summary infection control guidance for ambulance services during an influenza pandemic. 2009.
249. The Healthcare Infection Control Practices Advisory Committee (HICPAC) and The Centres for Disease Control (CDC). Core Infection Prevention and Control Practices for Safe Healthcare Delivery in All Settings – Recommendations of the Healthcare Infection Control Practices Advisory Committee. 2017.
250. Siegel JD, Rhinehart E, Jackson M, et al. 2007 guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *American Journal of Infection Control* 2007; 35: S65-S164.
251. Leung N, Chu DKW, Shiu E, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nature Medicine* 2020.
252. Johnson DF, Druce JD, Birch C, et al. A quantitative assessment of the efficacy of surgical and N95 masks to filter influenza virus in patients with acute influenza infection. *Clin Infect Dis* 2009; 49: 275-277. 2009/06/16. DOI: 10.1086/600041.
253. Su WL, Hung PP, Lin CP, et al. Masks and closed-loop ventilators prevent environmental contamination by COVID-19 patients in negative-pressure environments. *J Microbiol Immunol Infect* 2020 2020/05/20. DOI: 10.1016/j.jmii.2020.05.002.
254. Association of periOperative Registered Nurses (AORN). Recommended Practices for Prevention of Transmissible Infections in the Perioperative Practice Setting, (2007).

255. Association for Professionals in Infection control and Epidemiology (APIC), American Nurses Association, Association of Occupational Health Professionals in Healthcare, et al. Do's and don'ts for wearing procedure masks in non-surgical healthcare settings. 2015.
256. Loveday HP, Wilson JA, Pratt RJ, et al. epic3: National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England. *Journal of Hospital Infection* 2014; 86: S1-S70.
257. Occupational Safety and Health Administration (OSHA). Guidance on Preparing Workplaces for an Influenza Pandemic. 2009.
258. Gemmell L, Birks R, Radford P, et al. Infection control in anaesthesia. *Anaesthesia* 2008; 63: 1027-1036. Review.
259. Health and Safety Executive. The Control of Substances Hazardous to Health Regulations 2002. 2013.
260. UK Government. The Personal Protective Equipment Regulations 2002. 2002.
261. Coia JE, Ritchie L and Fry C. Use of Respiratory and facial protection. *Nursing Times* 2014; 110: 18-20.
262. Coia JE, Ritchie L, Adisesh A, et al. Guidance on the use of respiratory and facial protection equipment. *Journal of Hospital Infection* 2013; 85: 170-182. Short Survey.
263. Bunyan D, Ritchie L, Jenkins D, et al. Respiratory and facial protection: A critical review of recent literature. *Journal of Hospital Infection* 2013; 85: 165-169. Review.
264. MacIntyre CR, Seale H, Dung TC, et al. A cluster randomised trial of cloth masks compared with medical masks in healthcare workers. *BMJ Open* 2015; 5: e006577. Randomized Controlled Trial Research Support, Non-U.S. Gov't.
265. Health and Safety Executive. Respiratory protection equipment at work. A practical guide. 2013.
266. Offeddu V, Yung CF, Low MSF, et al. Effectiveness of Masks and Respirators Against Respiratory Infections in Healthcare Workers: A Systematic Review and Meta-Analysis. *Clin Infect Dis* 2017; 65: 1934-1942. 2017/11/16. DOI: 10.1093/cid/cix681.
267. Seto WH, Tsang D, Yung RW, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 2003; 361: 1519-1520. 2003/05/10. DOI: 10.1016/s0140-6736(03)13168-6.
268. Bartoszko JJ, Farooqi MAM, Alhazzani W, et al. Medical Masks vs N95 Respirators for Preventing COVID-19 in Health Care Workers A Systematic Review and Meta-Analysis of Randomized Trials. *Influenza Other Respir Viruses* 2020 2020/04/05. DOI: 10.1111/irv.12745.
269. Greenhalgh T, Chan XH, Khunti K, et al. What is the efficacy of standard face mask compared to respirator masks in preventing COVID-type respiratory illnesses in primary care staff? 30 March 2020 2020. Oxford COVID-19 Evidence Service Team.
270. Verbeek JH, Rajamaki B, Ijaz S, et al. Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff. *Cochrane Database Syst Rev* 2020; 4: CD011621. 2020/04/16. DOI: 10.1002/14651858.CD011621.pub4.

271. Scottish Government. COVID-19: Interim guidance on the extended use of medical masks and face coverings in hospitals and care homes. 23 June 2020 2020.
272. Health Protection Scotland. National Infection Prevention and Control Manual - Chapter 2 (Transmission-based precautions). Accessed 13 March 2020 2020. Health Protection Scotland.
273. Public Health England. COVID-19: infection prevention and control. 2 April 2020 2020.
274. ECRI. Safety of extended use and reuse of N95 respirators - Clinical evidence assessment. March 2020 2020. ECRI.
275. Bedell K, Buchaklian AH and Perlman S. Efficacy of an Automated Multiple Emitter Whole-Room Ultraviolet-C Disinfection System Against Coronaviruses MHV and MERS-CoV. *Infect Control Hosp Epidemiol* 2016; 37: 598-599. 2016/01/29. DOI: 10.1017/ice.2015.348.
276. Hamzavi IH, Lyons AB, Kohli I, et al. Ultraviolet germicidal irradiation: possible method for respirator disinfection to facilitate reuse during COVID-19 pandemic. *J Am Acad Dermatol* 2020 2020/04/05. DOI: 10.1016/j.jaad.2020.03.085.
277. Mills D, Harnish DA, Lawrence C, et al. Ultraviolet germicidal irradiation of influenza-contaminated N95 filtering facepiece respirators. *Am J Infect Control* 2018; 46: e49-e55. 2018/04/22. DOI: 10.1016/j.ajic.2018.02.018.
278. van Straten B, de Man P, van den Dobbelsteen J, et al. Sterilization of disposable face masks by means of standardized dry and steam sterilization processes; an alternative in the fight against mask shortages due to COVID-19. *Journal of Hospital Infection* 2020; Pre-proof.
279. Bergman M, Viscusi D, Heimbuch BK, et al. Evaluation of Multiple (3-Cycle) Decontamination Processing for Filtering Facepiece Respirators. 2010 2020; 5.
280. Cadnum JL, Li DF, Redmond SN, et al. Effectiveness of Ultraviolet-C Light and a High-Level Disinfection Cabinet for Decontamination of N95 Respirators. *Pathog Immun* 2020; 5: 52-67. 2020/05/05. DOI: 10.20411/pai.v5i1.372.
281. Fischer RJ, Morris DH, van Doremalen N, et al. Effectiveness of N95 Respirator Decontamination and Reuse against SARS-CoV-2 Virus. *Emerg Infect Dis* 2020; 26 2020/06/04. DOI: 10.3201/eid2609.201524.
282. ECDC. Infection prevention and control and preparedness for COVID-19 in healthcare settings. Second update - 31 March 2020. 2020.
283. MacIntyre CR, Wang Q, Cauchemez S, et al. A cluster randomized clinical trial comparing fit-tested and non-fit-tested N95 respirators to medical masks to prevent respiratory virus infection in health care workers. *Influenza Other Respir Viruses* 2011; 5: 170-179. 2011/04/12. DOI: 10.1111/j.1750-2659.2011.00198.x.
284. World Health Organization. Rational use of personal protective equipment for coronavirus disease 2019 (COVID-19) -Interim Guidance. 27 February 2020 2020. World Health Organization.
285. Kratzel A, Todt D, V'Kovski P, et al. Inactivation of Severe Acute Respiratory Syndrome Coronavirus 2 by WHO-Recommended Hand Rub Formulations and Alcohols. *Emerg Infect Dis* 2020; 26 2020/04/15. DOI: 10.3201/eid2607.200915.

286. Rabenau HF, Kampf G, Cinatl J, et al. Efficacy of various disinfectants against SARS coronavirus. *J Hosp Infect* 2005; 61: 107-111. 2005/06/01. DOI: 10.1016/j.jhin.2004.12.023.
287. Ong SWX, Tan YK, Chia PY, et al. Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient. *JAMA* 2020 2020/03/05. DOI: 10.1001/jama.2020.3227.
288. Ye G, Lin H, Chen S, et al. Environmental contamination of SARS-CoV-2 in healthcare premises. *J Infect* 2020 2020/05/04. DOI: 10.1016/j.jinf.2020.04.034.
289. Nelson A, Kassimatis J, Estoque J, et al. Environmental Detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) from Medical Equipment in Long-Term Care Facilities undergoing COVID-19 Outbreaks. *Am J Infect Control* 2020 2020/07/10. DOI: 10.1016/j.ajic.2020.07.001.
290. Colaneri M, Seminari E, Novati S, et al. Severe acute respiratory syndrome coronavirus 2 RNA contamination of inanimate surfaces and virus viability in a health care emergency unit. *Clin Microbiol Infect* 2020 2020/05/26. DOI: 10.1016/j.cmi.2020.05.009.
291. Ryu BH, Cho Y, Cho OH, et al. Environmental contamination of SARS-CoV-2 during the COVID-19 outbreak in South Korea. *Am J Infect Control* 2020 2020/06/03. DOI: 10.1016/j.ajic.2020.05.027.
292. Lee SE, Lee DY, Lee WG, et al. Detection of Novel Coronavirus on the Surface of Environmental Materials Contaminated by COVID-19 Patients in the Republic of Korea. *Osong Public Health Res Perspect* 2020; 11: 128-132. 2020/06/13. DOI: 10.24171/j.phrp.2020.11.3.03.
293. Cheng VC, Wong SC, Chan VW, et al. Air and environmental sampling for SARS-CoV-2 around hospitalized patients with coronavirus disease 2019 (COVID-19). *Infect Control Hosp Epidemiol* 2020: 1-32. 2020/06/09. DOI: 10.1017/ice.2020.282.
294. Chan KH, Sridhar S, Zhang RR, et al. Factors affecting stability and infectivity of SARS-CoV-2. *J Hosp Infect* 2020 2020/07/12. DOI: 10.1016/j.jhin.2020.07.009.
295. Kampf G, Todt D, Pfaender S, et al. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *Journal of Hospital Infection* 2020. Review.
296. Booth TF, Kournikakis B, Bastien N, et al. Detection of airborne severe acute respiratory syndrome (SARS) coronavirus and environmental contamination in SARS outbreak units. *J Infect Dis* 2005; 191: 1472-1477. 2005/04/06. DOI: 10.1086/429634.
297. Dowell SF, Simmerman JM, Erdman DD, et al. Severe acute respiratory syndrome coronavirus on hospital surfaces. *Clin Infect Dis* 2004; 39: 652-657. 2004/09/10. DOI: 10.1086/422652.
298. Chan KH, Peiris JS, Lam SY, et al. The Effects of Temperature and Relative Humidity on the Viability of the SARS Coronavirus. *Adv Virol* 2011; 2011: 734690. 2012/02/09. DOI: 10.1155/2011/734690.
299. van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. *N Engl J Med* 2020 2020/03/18. DOI: 10.1056/NEJMc2004973.

300. Warnes SL, Little ZR and Keevil CW. Human Coronavirus 229E Remains Infectious on Common Touch Surface Materials. *mBio* 2015; 6: e01697-01615. 2015/11/12. DOI: 10.1128/mBio.01697-15.
301. Carducci A, Federigi I, Liu D, et al. Making Waves: Coronavirus detection, presence and persistence in the water environment: State of the art and knowledge needs for public health. *Water Res* 2020; 179: 115907. 2020/05/12. DOI: 10.1016/j.watres.2020.115907.
302. Gundy P, Gerba C and Pepper I. Survival of coronaviruses in water and wastewater. *Food and Environmental Virology* 2009; 1: 10.
303. Wang J, Feng H, Zhang S, et al. SARS-CoV-2 RNA detection of hospital isolation wards hygiene monitoring during the Coronavirus Disease 2019 outbreak in a Chinese hospital. *Int J Infect Dis* 2020; 94: 103-106. 2020/04/21. DOI: 10.1016/j.ijid.2020.04.024.
304. Medema G, Heijnen L, Elsinga G, et al. Presence of SARS-Coronavirus-2 in sewage. *medRxiv* 2020; PRE-PRINT. DOI: <https://doi.org/10.1101/2020.03.29.20045880>
305. Wu FQ, Xiao A, Zhang JB, et al. SARS-CoV-2 titers in wastewater are higher than expected from clinically confirmed cases. *medRxiv* 2020; PRE-PRINT. DOI: <https://doi.org/10.1101/2020.04.05.20051540>.
306. Nemudryi A, Nemudraia A, Surya K, et al. Temporal detection and phylogenetic assessment of SARS-CoV-2 in municipal wastewater. *medRxiv* 2020; PRE-PRINT. DOI: <https://doi.org/10.1101/2020.04.15.20066746>.
307. Wurtzer S, Marechal V, Mouchel J, et al. Evaluation of lockdown impact on SARS-CoV-2 dynamics through viral genome quantification in Paris wastewaters. *medRxiv* 2020; PRE-PRINT. DOI: <https://doi.org/10.1101/2020.04.12.20062679>
308. La Rosa G, Bonadonna L, Lucentini L, et al. Coronavirus in water environments: Occurrence, persistence and concentration methods - A scoping review. *Water Res* 2020; 179: 115899. 2020/05/04. DOI: 10.1016/j.watres.2020.115899.
309. Geller C, Varbanov M and Duval RE. Human coronaviruses: insights into environmental resistance and its influence on the development of new antiseptic strategies. *Viruses* 2012; 4: 3044-3068. 2012/12/04. DOI: 10.3390/v4113044.
310. Reed NG. The history of ultraviolet germicidal irradiation for air disinfection. *Public Health Rep* 2010; 125: 15-27. 2010/04/21. DOI: 10.1177/003335491012500105.
311. Kovach CR, Taneli Y, Neiman T, et al. Evaluation of an ultraviolet room disinfection protocol to decrease nursing home microbial burden, infection and hospitalization rates. *BMC Infect Dis* 2017; 17: 186. 2017/03/04. DOI: 10.1186/s12879-017-2275-2.
312. Health Protection Scotland. Literature review and practice recommendations: existing and emerging technologies used for decontamination of the healthcare environment - Ultraviolet Light. 2016. Health Protection Scotland,.